(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
22 May 2003 (22.05.2003)

PCT

(10) International Publication Number
WO 03/042135 A2

(51) International Patent Classification[7]: C07C

(21) International Application Number: PCT/US02/35788

(22) International Filing Date:
8 November 2002 (08.11.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/336,939 9 November 2001 (09.11.2001) US

(71) Applicant: **THE PENN STATE RESEARCH FOUNDATION** [US/US]; 304 Old Main, University Park, PA 16802 (US).

(72) Inventors: **ZHANG, Xumu**; 276 Camelot Lane, State College, PA 16803 (US). **TANG, Wenjun**; 10 Vairo Boulevard, Apartment 27D, State College, PA 16803 (US).

(74) Agent: **GREELEY, Paul, D.**; Ohland, Greeley, Ruggiero & Perle, LLP, 10th floor, One Landmark Square, Stamford, CT 06901-2682 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/042135 A2

(54) Title: P-CHIRAL PHOSPHOLANES AND PHOSPHOCYCLIC COMPOUNDS AND THEIR USE IN ASYMMETRIC CATALYTIC REACTIONS

(57) Abstract: Chiral ligands and metal complexes based on such chiral ligands useful in asymmetric catalysis are disclosed. The metal complexes according to the present invention are useful as catalysts in asymmetric reactions, such as, hydrigenation, hydride transfer, allylic alkylation, hydrosilytation, hydroboration, hydrovinylation, hydroformylation, olefin metathesis, hydrocarboxylation, isomerization, cyclopropanation. Diels-Alder reaction, Heck reaction, isomerization, Aldol reaction, Michael addition; epoxidation, kinetic resolution and [m+n] cycloaddition. Processes for the preparation of the ligands are also described.

P-CHIRAL PHOSPHOLANES AND PHOSPHOCYCLIC COMPOUNDS AND THEIR USE IN ASYMMETRIC CATALYTIC REACTIONS

BACKGROUND OF THE INVENTION

1. FIELD OF THE INVENTION

The present invention relates to novel chiral ligands derived from P-chiral phospholanes and P-chiral phosphocyclic compounds and catalysts for applications in asymmetric catalysis. More particularly, the present invention relates to transition metal complexes of these chiral phosphine ligands, which are useful as catalysts in asymmetric reactions, such as, hydrogenation, hydride transfer, hydrocarboxylation, hydrosilylation, hydroboration, hydrovinylation, hydroformylation, allylic alkylation, olefin metathesis, isomerization, cyclopropanation, Diels-Alder reaction, Heck reaction, Aldol reaction, Michael addition, epoxidation, kinetic resolution and [m+n] cycloaddition.

2. DESCRIPTION OF THE PRIOR ART

Molecular chirality plays an important role in science and technology. The biological activities of many pharmaceuticals, fragrances, food additives and agrochemicals are often associated with their absolute molecular configuration. A growing demand in pharmaceutical and fine chemical industries is to develop cost-effective processes for the manufacture of single-enantiomeric products. To meet this challenge, chemists have explored many approaches for acquiring enantiomerically pure compounds ranging from optical resolution and

structural modification of naturally occurring chiral substances to asymmetric catalysis using synthetic chiral catalysts and enzymes. Among these methods, asymmetric catalysis is perhaps the most efficient because a small amount of a chiral catalyst can be used to produce a large quantity of a chiral target molecule [Book, Ojima, I., Ed. *Catalytic Asymmetric Synthesis*, VCH, New York, 1993 and Noyori, R. *Asymmetric Catalysis In Organic Synthesis*, John Wiley & Sons, Inc., New York, 1994].

Asymmetric hydrogenation accounts for major part of all asymmetric synthesis on a commercial scale. Some dramatic examples of industrial applications of asymmetric synthesis include Monsanto's L-DOPA synthesis (asymmetric hydrogenation of a dehydroamino acid, 94 % ee, 20,000 turnovers with a Rh-DIPAMP complex) [Knowles, W. S. *Acc. Chem. Res.* 1983, *16*, 106], Takasago's L-menthol synthesis (asymmetric isomerization, 98 %ee, 300,000 turnovers with a Rh-BINAP complex) [Noyori, R.; Takaya, H. *Acc. Chem. Res.* 1990, *23*, 345] and Norvatis' (S)-Metolachlor synthesis (asymmetric hydrogenation of an imine, 80 % ee, 1,000,000 turnovers with an Ir-ferrocenyl phosphine complex) [Spindler, F.; Pugin, B.; Jalett, H.-P., Buser, H.-P.; Pittelkow, U.; Blaser, H,-U., Altanta, 1996; Chem. Ind. (Dekker), 1996, 63 and Tongni, A. *Angew. Chem. Int. Ed. Engl.* 1996, *356*, 14575].

Invention of chiral ligands for transition metal-catalyzed reactions plays a critical role in asymmetric catalysis. Not only the enantioselectivity depends on the framework of chiral ligands, reactivities can often be altered by changing the steric and electronic structure of the ligands.

Since small changes in the ligand can influence the (delta)(delta)G of the rate-determining step, it is very hard to predict which ligand can be effective for any particular reaction or substrate. Accordingly, discovery

of new chiral ligands sets the foundation of highly enantioselective transition metal-catalyzed reactions.

In recent years, a large number of chiral ligands have been developed for use in asymmetric catalysis reactions. Despite this, only few chiral ligands have been found to be suitable for use in industry for the production of chiral molecules that require high selectivity.

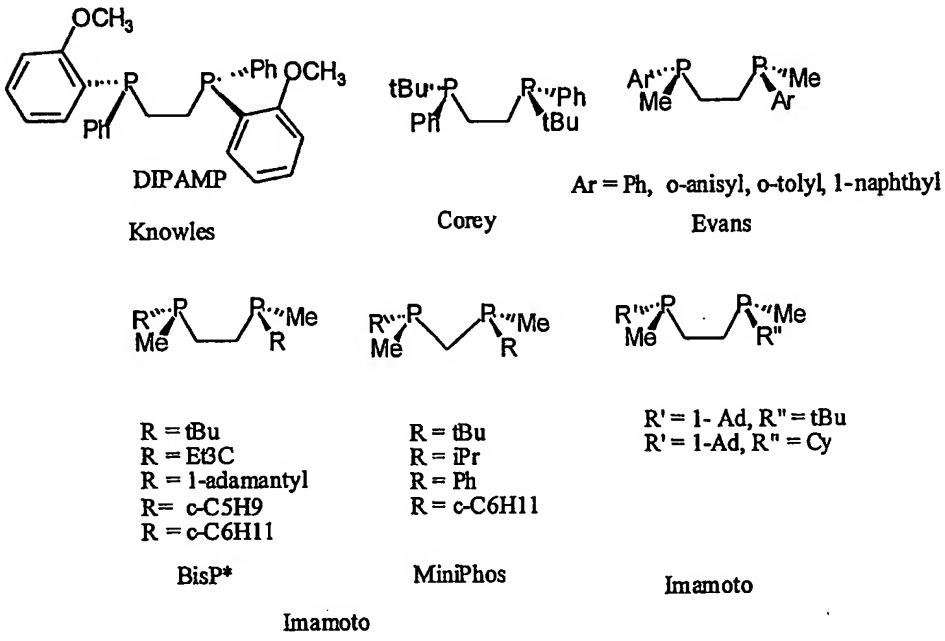
One of the earliest P-chiral phosphine ligands is DIPAMP, which was developed by Knowles, J. Am. Chem. Soc., 99, 5946 (1977). The Rh(I)-DIPAMP complex has been used in the synthesis of L-DOPA.

There are continuing efforts from many groups to develop strategies for making P-chiral ligands for asymmetric catalysis, including, for example, the following: I. Ojima, Ed., Catalytic Asymmetric Synthesis, 2nd ed., VCH publishers, Wheinheim, 2000. Juge and Genet, Tetrahedron Lett., 30, 6357 (1989), who have developed a method for making P-chiral phosphines. E. J. Corey, J. Am. Chem. Soc., 115, 11000 (1993), who has developed a method for preparing P-chiral phosphines and diphosphines. An enantioselective deprotonation as a method for the synthesis of P-chiral phosphines has been applied by Evans, J. Am. Chem. Soc., 117, 9075 (1995). Typically, phosphine-borane, phosphine sulfides have been used. Enantioselective deprotonation of these compounds and Cu-mediated coupling reactions can produce a number of diphosphines. A Cu-mediated coupling reaction was reported by Mislow, J. Am. Chem. Soc., 95, 5839 (1973). Formation of phosphine-borane and removal of borane have been reported by Imamoto, J. Am. Chem. Soc., 112, 5244 (1990), Yamago, J. Chem. Soc., Chem. Commun., 2093 (1994) and Livinghouse, Tetrahedron Lett., 35, 9319 (1994). Desulfurization of phosphine sulfides is reported by Mislow, J. Am. Chem., Soc., 91, 7023 (1969). More recently, Imamoto has successfully used these strategies to

make a number of P-chiral phosphines such as BisP*, J. Am. Chem. Soc., 123, 5268 (2001), MiniPhos, J. Org. Chem., 64, 2988 (1999) and other mixed P-chiral ligands, Org. Lett., 3, 373 (2001).

These ligands have been used effectively in many asymmetric reactions, especially in asymmetric hydrogenation reactions, such as those described in Adv. Synth. Catal., 343, 118 (2001).

Some of these ligands are depicted below:



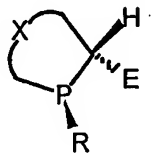
Despite the wide variation in the substituted groups in the above ligands, the majority of these ligands are derivatives of the DIPAMP ligand. A possible drawback of these ligands is that ligands having a DIPAMP structure are conformationally flexible and, as a result, enantioselectivity is difficult to optimize.

In contrast to the ligands of the prior art, the present invention provides a phospholane and phosphocyclic structure to restrict the conformational flexibility such that a high enantioselectivity can be achieved in the transition metal catalysts prepared from these ligands.

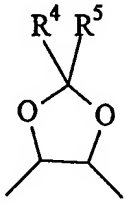
Thus, from a stereochemical point of view, additional stereogenic centers (e.g. four or more stereogenic centers) are typically created to make the novel ligands of the present invention substantially more selective in asymmetric catalytic reactions than, for example, the DIPAMP and BisP* ligands, which have only two stereogenic centers.

SUMMARY OF THE INVENTION

The present invention provides a chiral ligand represented by the following formula or its enantiomer:



wherein X is a divalent group selected from $(CR^4R^5)_n$, $(CR^4R^5)_n$-Z-$(CR^4R^5)_n$ and group represented by the formula:

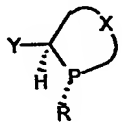


wherein each n is independently an integer from 1 to 6; wherein each R^4 and R^5 can independently be hydrogen, alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, halogen, hydroxy, alkoxy, aryloxy, alkylthio, arylthio and amido; and

wherein Z can be O, S, -COO-, -CO-, $O-(CR^4R^5)_n-O$, CH_2 (C_6H_4), CH_2 (Ar), CH_2(hetereoaryl), alkenyl, CH_2(alkenyl), C_5H_3N, divalent aryl, 2,2'-divalent-1,1'-biphenyl, SiR'_2, PR' and NR^6 wherein each of R' and R^6 can independently be hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, hydroxy, alkoxy, aryloxy, acyl and alkoxycarbonyl;

wherein R can be alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, alkoxy and aryloxy;

wherein E can be PR'_2, PR'R", o-substituted pyridine, oxazoline, chiral oxazoline, CH_2(chiral oxazoline), CR'2(chiral oxazoline), $CH_2PR'_2$, CH_2(o-substituted pyridine), SiR'_3, CR'_2OH and a group represented by the formula:



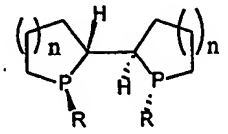
wherein Y can be

$(CR^4R^5)_m$ and $(CR^4R^5)_m-Z-(CR^4R^5)_m$;

wherein each m is independently an integer from 0 to 3; wherein each R^4 and R^5 can independently be hydrogen, alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, halogen, hydroxy, alkoxy, aryloxy, alkylthio, arylthio and amido; and wherein Z can be O, S, -CO-, -COO-, $O-(CR^4R^5)_n-O$, CH_2 (C_6H_4), CH_2 (Ar), CH_2(hetereoaryl), alkenyl, CH_2(alkenyl), C_5H_3N, divalent aryl, 2,2'-divalent-1,1'-biphenyl, SiR'_2, PR'

and NR^6 wherein each of R' and R^6 can independently be hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, hydroxy, alkoxy, aryloxy, acyl and alkoxycarbonyl.

More particularly, the present invention provides a chiral ligand represented by the formula and its enantiomer:



n = 0, 1, 2

wherein R can be alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, alkoxy and aryloxy; and

wherein n is from 0 to 2.

The present invention further provides a catalyst prepared by a process including:

contacting a transition metal salt, or a complex thereof, and a chiral ligand according to the present invention as described herein above.

The present invention still further provides a process for preparation of an asymmetric compound including:

contacting a substrate capable of forming an asymmetric product by an asymmetric reaction and a catalyst prepared by a process including: contacting a transition metal salt, or a complex thereof, and a chiral ligand according to the present invention as described herein above.

The present invention still further provides a process for preparing (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl -[2,2']-diphospholanyl-1,1'-disulfide including the steps of:

asymmetrically deprotonating a 1-alkyl-phospholane-1-sulfide with n-butyllithium/(-)-sparteine in a solvent to produce an anion of the 1-alkyl-phospholane-1-sulfide; and

contacting the anion of the 1-alkyl-phospholane-1-sulfide and $CuCl_2$ to oxidatively couple the anion of the 1-alkyl-phospholane-1-sulfide and produce a reaction mixture including the (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide.

Further still, the present invention provides a process for preparing (*1S, 1S', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl including the steps of:

asymmetrically deprotonating a 1-alkyl-phospholane-1-sulfide with n-butyllithium/(-)-sparteine in a solvent to produce an anion of the 1-alkyl-phospholane-1-sulfide;

contacting the anion of the 1-alkyl-phospholane-1-sulfide and $CuCl_2$ to oxidatively couple the anion of the 1-alkyl-phospholane-1-sulfide and produce a reaction mixture including (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide;

recrystallizing the (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide from the reaction mixture; and

contacting the (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide and hexachlorodisilane in a solvent to produce (*1S, 1S', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl.

The presence of additional stereogenic centers (e.g. four or more stereogenic centers) in the novel ligands of the present invention makes them substantially more selective in asymmetric catalytic reactions than, for example, the DIPAMP and BisP* ligands, which have only two stereogenic centers.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides novel P-chiral phospholane and phosphocyclic compounds and described their use in asymmetric catalysis.

Introduction of cyclic structures can restrict the rotation of substituents adjacent to the phosphines and control of orientations of these groups around phosphine can lead effective chiral induction for asymmetric reactions. Metal complexes of these phosphines, and related none C_2 symmetric ligands are useful for many asymmetric reactions.

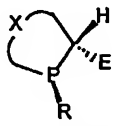
Tunability of ligand chiral environment is crucial for achieving high enantioselectivity. The steric and electronic structure of the conformationally rigid cyclic phosphines can be fine-tuned by variation of ring size and substituents.

Several new chiral phosphines are developed for asymmetric catalytic reactions. A variety of asymmetric reactions, such as, hydrogenation, hydride transfer, allylic alkylation, hydrosilylation, hydroboration, hydrovinylation, hydroformylation, olefin metathesis, hydrocarboxylation, isomerization, cyclopropanation, Diels-Alder reaction, Heck reaction, isomerization, Aldol reaction, Michael addition, epoxidation, kinetic resolution and [m+n] cycloaddition were developed with these chiral ligands systems.

The ligands of the present invention can be a racemic mixture of enantiomers. Preferably, the ligand is a non-racemic mixture of enantiomers, and more preferably, the ligand is one of the enantiomers.

Preferably, the ligand has an optical purity of at least 85% ee, and more preferably, the ligand has an optical purity of at least 95% ee.

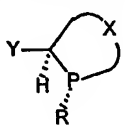
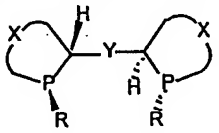
Representative examples of chiral ligands of the current invention are shown below. A number of chiral ligands with desired structures according to the present invention can be made and used in the preparation of the catalysts described in the present invention.



X = $(CH_2)_n$, n = 1, 2, 3, 4, 5, 6. CH_2OCH_2, CH_2NHCH_2,, $CH_2CH(R')CH(R')$, $CH_2CH(OR')CH(OR')$, $CH_2CH(OH)CH(OH)$, $CH_2CH(OCR'_2O)CH$, $CH_2CH(OalkylO)CH$, $CH_2CH(OCHR'O)CH$, $CH_2NR'CH_2$, $CH_2CH_2NR'CH_2$, $CH_2CH_2OCH_2$, $CH_2(C_6H_4)$, $CH_2(Ar)$, CH_2(hetereoaryl), CH_2(alkenyl), alkyl, substituted alkyl, aryl, substituted aryl, CH_2(biaryl), CH_2(ferrocene).

R = alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocene

E = PR'_2, PR'R", o-substituted pyridine, oxazoline, chiral oxazoline, CH_2(chiral oxazoline), CR'_2(chiral oxazoline), $CH_2PR'_2$, CH_2(o-substituted pyridine), SiR'_3, CR'_2OH

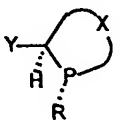
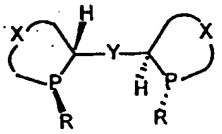
or E =  then ligands are: 

Y = $(CH_2)_n$, n = 0, 1, 2, 3, CH_2NHCH_2, CR'_2, CO, SiR'_2, C_5H_3N, C_6H_4, alkyl, substituted alkyl, divalent aryl, 2,2'divalent-1,1'biphenyl, substitued aryl, hetereoaryl, ferrocene

R' = alkyl, aryl, substituted alkyl, aryl, alkylaryl, H.

In these ligands, the bridge group X for the phosphocyclic compounds are (CH2)n, n = 1, 2, 3, 4, 5, 6. CH2OCH2, CH2NHCH2,, CH2CH(R')CH(R'), CH2CH(OR')CH(OR'), CH2CH(OH)CH(OH), CH2CH(OCR'2O)CH, CH2CH(OalkylO)CH, CH2CH(OCHR'O)CH, CH2NR'CH2, CH2CH2NR'CH2, CH2CH2OCH2, CH2(C6H4), CH2(Ar), CH2(hetereoaryl), CH2(alkenyl), alkyl, substituted alkyl, aryl, substituted aryl, CH2(biaryl), CH2(ferrocene). R is alkyl, aryl, substituted alkyl,

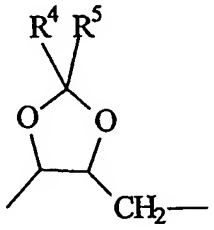
substituted aryl, hetereoaryl, ferrocene. E is PR'2, PR'R", o-substituted pyridine, oxazoline, chiral oxazoline, CH2(chiral oxazoline), CR'2(chiral oxazoline), CH2PR'2, CH2(o-substituted pyridine), SiR'3, CR'2OH.

E =  then ligands are: 

Y can be (CH2)n, n = 0, 1, 2, 3, CH2NHCH2, CH2SCH2, CH2PR'CH2, CR'2, CO, SiR'2, C5H3N, C6H4, alkyl, substituted alkyl, divalent aryl, 2,2'divalent-1,1'biphenyl, substituted aryl, hetereoaryl, ferrocene. R' = alkyl, aryl, substituted alkyl, aryl, alkylaryl, H.

In a preferred embodiment, the ligand of the present invention includes compounds represented by the formulas wherein:

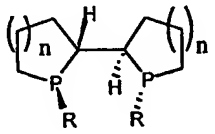
X can be $(CH_2)_n$ wherein n is from 1 to 6, CH_2OCH_2, CH_2NHCH_2, $CH_2CH(R')CH(R')$, $CH_2CH(OR')CH(OR')$, $CH_2NR'CH_2$, $CH_2CH(OH)CH(OH)$, $CH_2CH_2NR'CH_2$, $CH_2CH_2OCH_2$ and a group represented by the formula:



wherein each R^4 and R^5 can independently be hydrogen, alkyl, aryl, substituted alkyl and substituted aryl; and wherein:

Y can be $(CH_2)_n$ wherein n is from 0 to 3, CH_2NHCH_2, CH_2SCH_2, $CH_2PR'CH_2$, CR'2, CO, SiR'_2, C_5H_3N, C_6H_4, alkylene, substituted alkylene, 1,2-divalent arylene, 2,2'-divalent-1,1'-biphenyl, substituted aryl, hetereoaryl and ferrocene.

More particularly, the chiral ligand can be represented by the formula and its enantiomer:



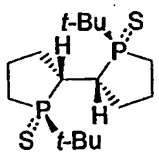
n = 0, 1, 2

wherein R can be alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, alkoxy and aryloxy; and

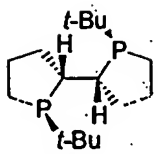
wherein n is from 0 to 2;

R can be CH_3, Et, iPr, t-Bu, 1-adamantyl, Et_3C, cyclo-C_5H_9, cyclo-C_6H_{11}, phenyl, p-tolyl, 3,5-dimethylphenyl, 3,5-di-t-butyl phenyl, ortho-anisyl and naphthyl.

Examples of such ligands include a ligand represented by the formula and its enantiomer:



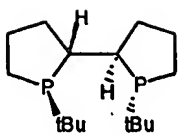
and a ligand represented by the formula and its enantiomer:



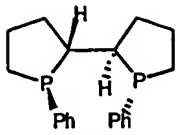
The ligands according to the present invention can be in the form of a phosphine borane, phosphine sulfide or phosphine oxide.

Selective examples of specific chiral ligands are listed below to illustrate the new P-chiral phospholanes and P-chiral phosphocyclic compounds (L1 to L35).

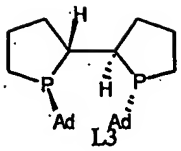
For each ligand, the corresponding enantiomer is also contemplated. These compounds can be prepared from corresponding phosphine-boranes, phosphine sulfides and phosphine oxides.



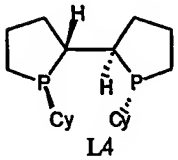
L1



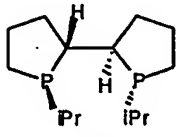
L2



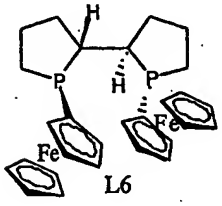
L3



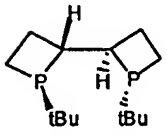
L4



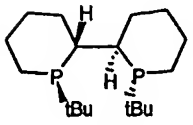
L5



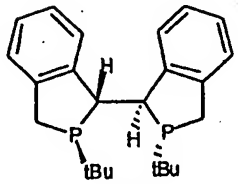
L6



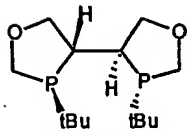
L7



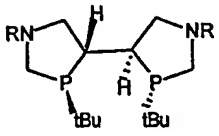
L8



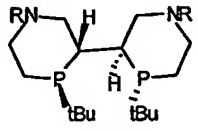
L9



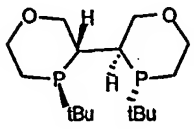
L10



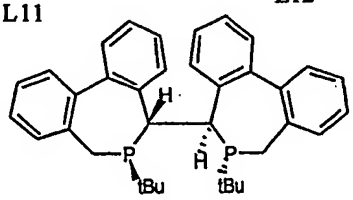
L11



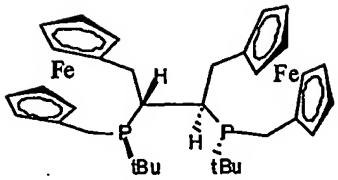
L12



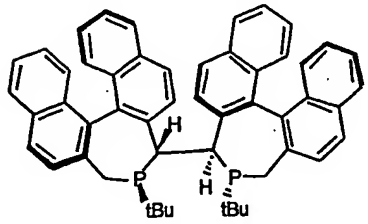
L13



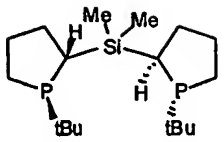
L14



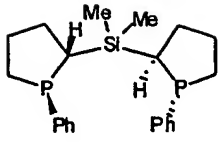
L15



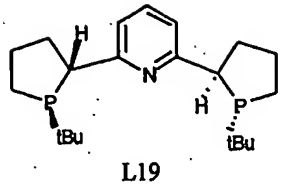
L16



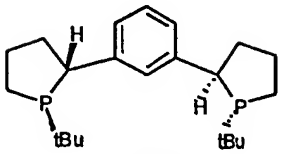
L17



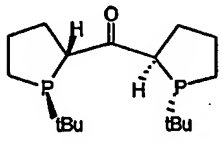
L18



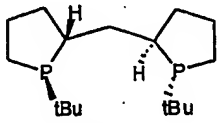
L19



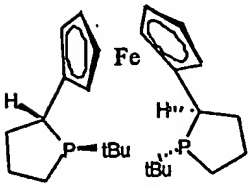
L20



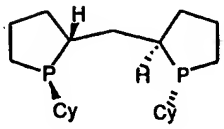
L21



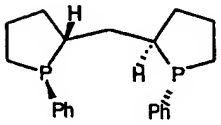
L22



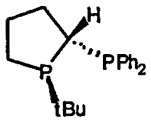
L23



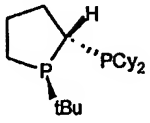
L24



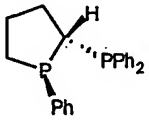
L25



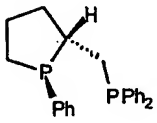
L26



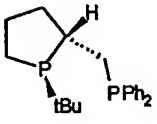
L27



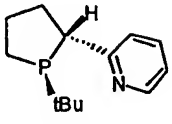
L28



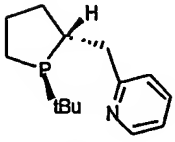
L29



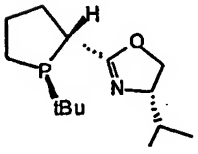
L30



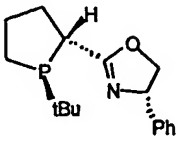
L31



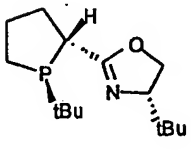
L32



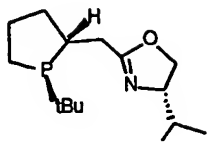
L33



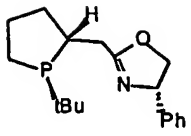
L34



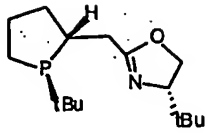
L35



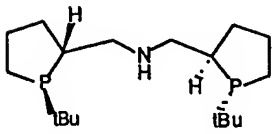
L36



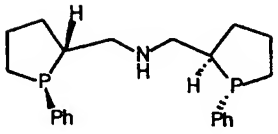
L37



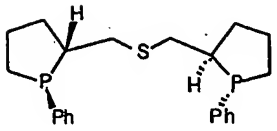
L38



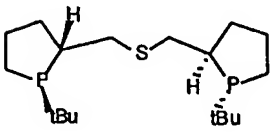
L39



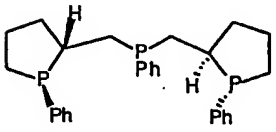
L40



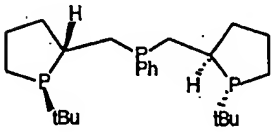
L41



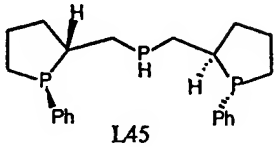
L42



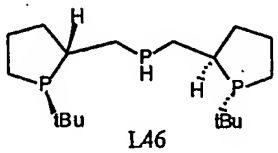
L43



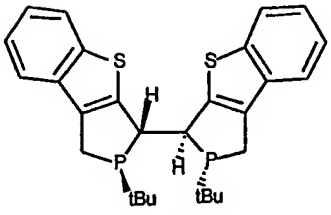
L44



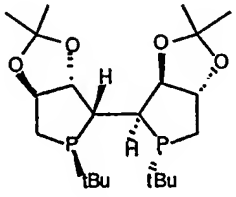
L45



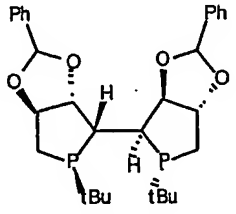
L46



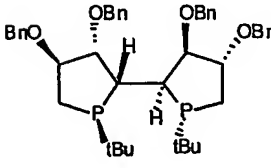
L47



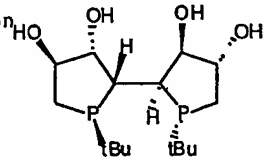
L48



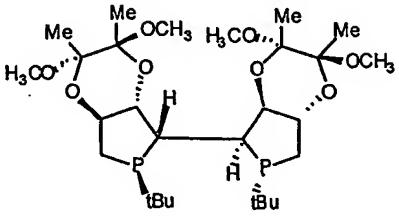
L49



L50



L51



L52

5

Since Ir-catalyzed asymmetric hydrogenation is still highly substrate-dependent, development of new efficient chiral ligands for Ir-catalyzed hydrogenation is a continuing challenge. After development of phosphinooxazoline ligands for Ir-catalyzed asymmetric hydrogenation, Pfaltz and others have continued their efforts for the search of new efficient P, N ligands (A. Lightfoot, P. Schnider, A. Pfaltz, *Angew. Chem. Int. Ed.* **1998**, *37*, 2897-2899). Various P, N ligands such as TADDOL-phosphite-oxazoline, PyrPHOX, and phosphinite-oxazoline were subsequently developed by Pfaltz and coworkers (J. Blankenstein, A. Pfaltz, *Angew. Chem. Int. Ed.* **2001**, *40*, 4445-4447). Burgess also reported JM-Phos and imidazolylidene-oxazoline (D.-R. Hou, J. H. Reibenspies, K. Burgess, *J. Org. Chem.* **2001**, *66*, 206-215; M. T. Powell, D.-R. Hou, M. C. Perry, X. Cui, K. Burgess, J. *Am. Chem. Soc.* **2001**, *123*, 8878-8879).

In this invention, we also report a new class of chiral P, N ligands, the phospholane-oxazolines, for Ir-catalyzed asymmetric hydrogenation. Excellent enantioselecitivities have been obtained in hydrogenation of methylstilbenes and methylcinammic esters.

The present invention further provides a catalyst prepared by a process including:

contacting a transition metal salt, or a complex thereof, and a chiral ligand according to the present invention as described herein above.

Suitable transition metals for the preparation of the catalyst include Ag, Pt, Pd, Rh, Ru, Ir, Cu, Ni, Mo, Ti, V, Re and Mn.

As mentioned above, the catalyst can be prepared by contacting a transition metal salt or its complex and a ligand according to the present invention.

Suitable transition metal salts or complexes include the following:

AgX; Ag(OTf); $Ag(OTf)_2$; AgOAc; $PtCl_2$; H_2PtCl_4; $Pd_2(DBA)_3$; $Pd(OAc)_2$; $PdCl_2(RCN)_2$; $(Pd(allyl)Cl)_2$; $Pd(PR_3)_4$; $(Rh(NBD)_2)X$; $(Rh(NBD)Cl)_2$; $(Rh(COD)Cl)_2$; $(Rh(COD)_2)X$; $Rh(acac)(CO)_2$; $Rh(ethylene)_2(acac)$; $(Rh(ethylene)_2Cl)_2$; $RhCl(PPh_3)_3$; $Rh(CO)_2Cl_2$; $RuHX(L)_2$(diphosphine), $RuX_2(L)_2$ (diphosphine), Ru(arene)X_2(diphosphine), Ru(aryl group)X_2; $Ru(RCOO)_2$(diphosphine); Ru(methallyl)2(diphosphine); Ru(aryl group)$X_2(PPh_3)_3$; Ru(COD)(COT); Ru(COD)(COT)X; RuX_2(cymen); $Ru(COD)_n$; Ru(aryl group)X_2(diphosphine); $RuCl_2$(COD); $(Ru(COD)_2)X$; RuX_2(diphosphine); $RuCl_2(=CHR)(PR'_3)_2$; $Ru(ArH)Cl_2$; Ru(COD)(methallyl)$_2$; $(Ir(NBD)_2Cl)_2$; $(Ir(NBD)_2)X$; $(Ir(COD)_2Cl)_2$; $(Ir(COD)_2)X$; CuX $(NCCH_3)_4$; Cu(OTf); $Cu(OTf)_2$; Cu(Ar)X; CuX; $Ni(acac)_2$; NiX_2; $(Ni(allyl)X)_2$; $Ni(COD)_2$; $MoO_2(acac)_2$; $Ti(OiPr)_4$; $VO(acac)_2$; $MeReO_3$; MnX_2 and $Mn(acac)_2$.

Each R and R' in these is independently selected from alkyl or aryl; Ar is an aryl group; and X is a counteranion.

In the above transition metal salts and complexes, L is a solvent and the counteranion X can be halogen, BF_4, $B(Ar)_4$ wherein Ar is fluorophenyl or 3,5-di-trifluoromethyl-1-phenyl, ClO_4, SbF_6, PF_6, CF_3SO_3, RCOO or a mixture thereof.

In another aspect, the present invention includes a process for preparation of an asymmetric compound using the catalysts described above. The process includes the step of contacting a substrate capable of forming an asymmetric product by an asymmetric reaction and a catalyst according to the present invention prepared by contacting a

transition metal salt, or a complex thereof, and a ligand according to the present invention.

Suitable asymmetric reactions include asymmetric hydrogenation, hydride transfer, allylic alkylation, hydrosilylation, hydroboration, hydrovinylation, hydroformylation, olefin metathesis, hydrocarboxylation, isomerization, cyclopropanation, Diels-Alder reaction, Heck reaction, isomerization, Aldol reaction, Michael addition; epoxidation, kinetic resolution and [m+n] cycloaddition wherein m = 3 to 6 and n = 2.

Preferably, the asymmetric reaction is hydrogenation and the substrate to be hydrogenated is an ethylenically unsaturated compound, imine, ketone, enamine, enamide, and vinyl ester.

The present invention still further includes a process for preparation of an asymmetric compound including:

contacting a substrate capable of forming an asymmetric product by an asymmetric reaction and a catalyst prepared by a process including: contacting a transition metal salt, or a complex thereof, and a chiral ligand according to the present invention as described herein above.

The present invention still further includes a process for preparing (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl -[2,2']-diphospholanyl-1,1'-disulfide including the steps of:

asymmetrically deprotonating a 1-alkyl-phospholane-1-sulfide with n-butyllithium/(-)-sparteine in a solvent to produce an anion of the 1-alkyl-phospholane-1-sulfide; and

contacting the anion of the 1-alkyl-phospholane-1-sulfide and $CuCl_2$ to oxidatively couple the anion of the 1-alkyl-phospholane-1-sulfide and produce a reaction mixture including the (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide.

Further still, the present invention includes a process for preparing (*1S, 1S', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl.

The process includes the steps of:

asymmetrically deprotonating a 1-alkyl-phospholane-1-sulfide with n-butyllithium/(-)-sparteine in a solvent to produce an anion of the 1-alkyl-phospholane-1-sulfide;

contacting the anion of the 1-alkyl-phospholane-1-sulfide and $CuCl_2$ to oxidatively couple the anion of the 1-alkyl-phospholane-1-sulfide and produce a reaction mixture comprising (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide;

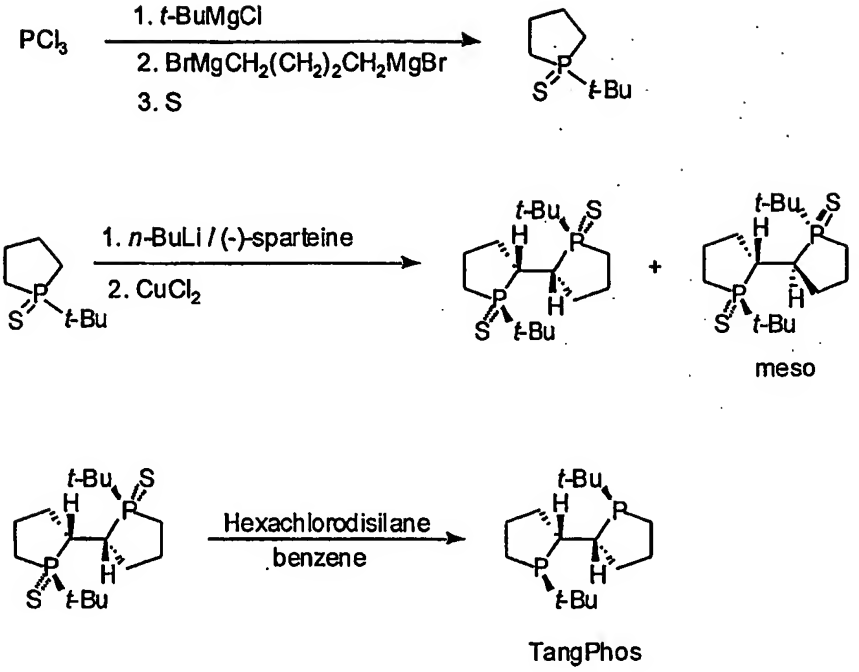
recrystallizing the (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide from the reaction mixture; and

contacting the (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide and hexachlorodisilane in a solvent to produce (*1S, 1S', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl.

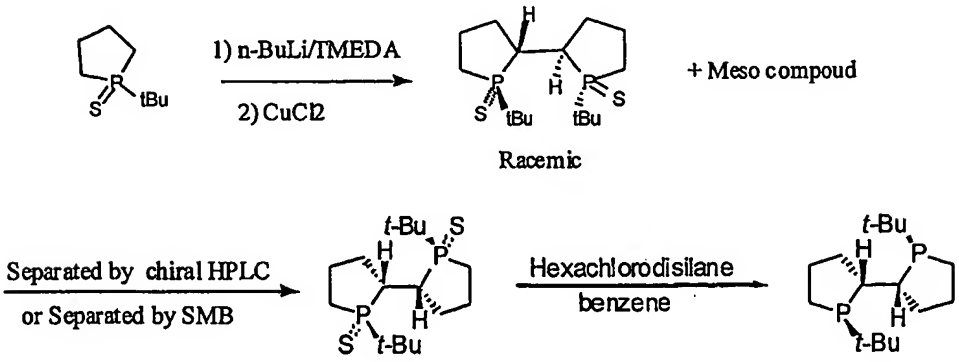
Preferably, (*1S, 1S', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl is (*1S, 1S', 2R, 2R'*)-1,1'-di-*tert*-butyl-[2,2']-diphospholanyl, which is prepared from suitable *tert*-butyl group containing starting materials.

Several suitable procedures to prepare the chiral ligands according to the present invention are described herein below.

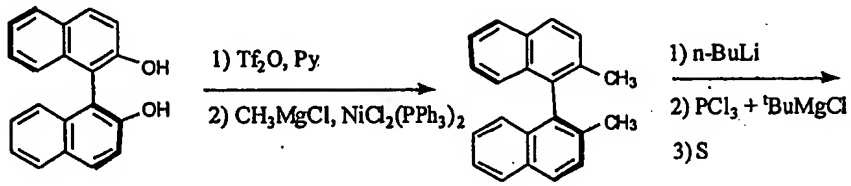
(a) Synthesis of TangPhos using asymmetric deprotonation

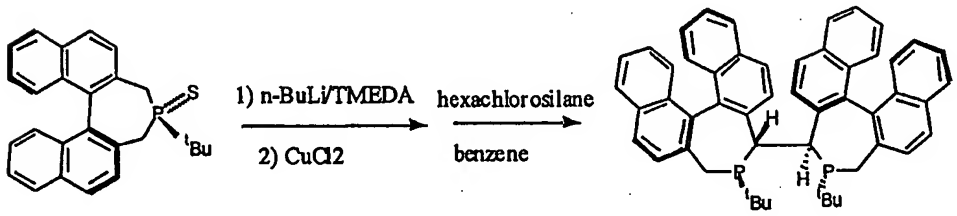


(b) Synthesis of TangPhos through chiral separation

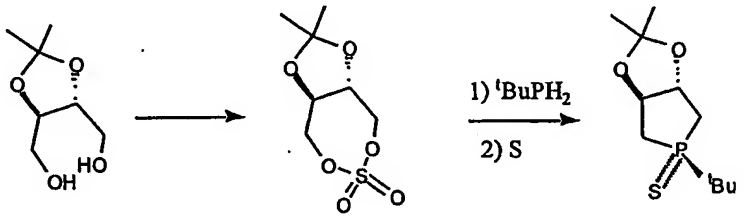


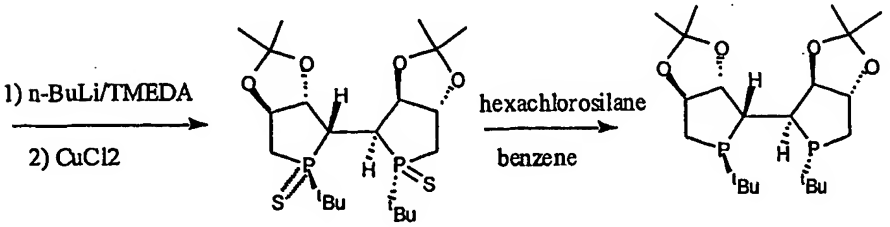
(c) Synthesis of TangPhos ligands through utilization of backbone chirality



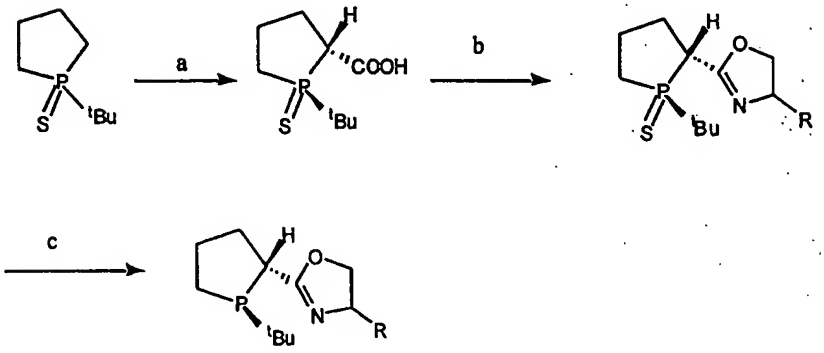


(d) Synthesis of TangPhos Ligands through a chiral pool method





(e) Synthesis of PN ligands for asymmetric catalysis



(a) nBuLi, Sparteine, CO_2; (b) amino alcohol, EDC, HOBT, DMF, then MsCl; (c) Raney Ni

General procedures

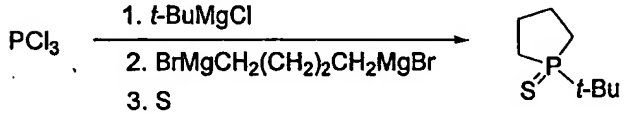
All reactions and manipulations were performed in a nitrogen-filled glovebox or using standard Schlenk techniques. THF and toluene were dried and distilled from sodium-benzophenone ketyl under nitrogen. Methylene chloride was distilled from CaH_2. Methanol was distilled from Mg under nitrogen. (R, R)-BDNPB was made a solution of 10mg/ml in toluene before use. Column chromatography was performed using EM silica gel 60 (230~400 mesh). ^{1}H, ^{13}C and ^{31}P NMR were recorded on Bruker WP-200, AM-300, and AMX-360 spectrometers. Chemical shifts were reported in ppm down field from tetramethylsilane with the solvent resonance as the internal standard. Optical rotation was obtained on a Perkin-Elmer 241 polarimeter. MS spectra were recorded on a KRATOS mass spectrometer MS 9/50 for LR-EI and HR-EI. GC analysis was carried on Helwett-Packard 6890 gas chromatography using chiral

capillary columns. HPLC analysis was carried on Waters™ 600 chromatography.

EXAMPLE 1: Synthesis of TangPhos (1)

An efficient three-step synthetic of chiral C2 symmetric P-chiral bisphospholane route has been developed.

Preparation of 1-*tert*-butyl-phospholane 1-sulfide

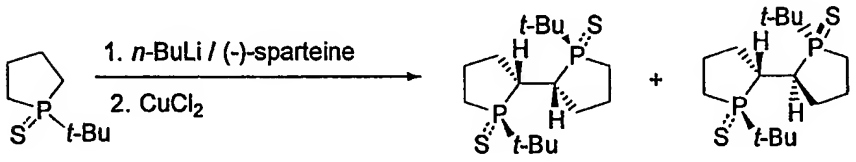


Preparation of $BrMgCH_2(CH_2)_2CH_2MgBr$. To a dry Schlenk flask held with magnesium turning (7.92 g, 0.33 mol) in 300 ml dry THF was added dropwise 1,4-dibromobutane (23.7 g, 0.11 mol) in 50 mL of THF at room temperature. The reaction was very exothermic during the addition. After the addition was complete (within 1h), the resulting dark solution was kept at r.t. for 2 more hours. The whole solution was used directly for the following reaction.

To a solution of phosphorous trichloride (13.7 g, 0.10 mol) in THF (300 mL) was added dropwise a solution of *t*-BuMgCl in THF (100 mL, 1.0M) at –78°C. The addition was complete within 2 hrs. After the mixture was stand at –78°C for 1 h, a solution of $BrMgCH_2(CH)_2CH_2MgBr$ in THF (made above) was added dropwise. The addition was complete within 2 hrs. The mixture was then allowed to warm to r. t over 2 h and stirred overnight.

At room temperature, to the reaction mixture was added sulfur powder (4.8g, 0.15 mol) through one portion. The resulting solution was further stirred at r.t. for 2 h. Water (300 mL) was then added. To the THF layer was added 500 mL EtOAc. The organic layer was washed with water (300 mL) followed by brine (300 mL), dried over Na_2SO_4, and concentrated. The resulting oil was passed through a silica gel column followed by recrystallization to give colorless crystalline product 1-*tert*-butyl-phospholane 1-sulfide 8g (45% yield).

Synthesis of (*1R, 1R', 2R, 2R'*)-1, 1'-di-*tert*-butyl-[2,2']-diphospholanyl 1, 1'-disulfide

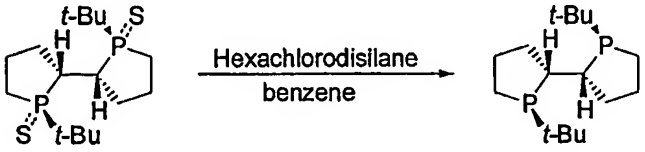


At –78°C, to a solution of (-)-sparteine (7.83 mL, 34 mmol) in ether (200 mL) was added n-butyllithium (21.3 mL, 34 mmol, 1.6M in hexane) dropwise. The resulting solution was kept at –78°C for 30 min. Then at this temperature, to the solution was added dropwise a solution of 1-*tert*-butyl-phospholane 1-sulfide (5.0 g, 28.4 mmol in ether (100 mL). The addition was complete within 1hr. The resulting mixture was kept at –78°C and stirred for 8 more hrs. Then dry $CuCl_2$ (5.73 g, 42.6 mmol) was added into the solution through one portion. The resulting suspension was vigorously stirred and allowed to warm to r. t. over 4hrs. 150ml of concentrated ammonia was added. The water layer was washed twice

with EtOAc (2 x 100 mL). The combined organic phase was further washed in a sequence with 5% ammonia (100 mL), 1N HCl (100 mL), water (100 mL), and brine (100 mL). After dried over Na_2SO_4, the solution was concentrated under reduced pressure to give an oily solid, which was subsequently purified by passing a silica gel column to give a solid mixture (4 g) of (*1R, 1R', 2R, 2R'*)-1, 1'-di-*tert*-butyl-[2,2']-diphospholanyl 1, 1'-disulfide (72% ee, 83%) and meso compound (1R, 1R', 2S, 2S')-1, 1'-di-*tert*-butyl-[2,2']-diphospholanyl 1, 1'-disulfide (17%).

The mixture was recrystallized from ethyl acetate and ethanol to give 700mg of pure product (1R, 1R', 2R, 2R')-1, 1'-di-*tert*-butyl-[2,2']-diphospholanyl 1, 1'-disulfide (ee: >99% according to HPLC, total yield: 14%).

Synthesis of (*1S, 1S', 2R, 2R'*)-1, 1'-di-*tert*-butyl-[2,2']-diphospholanyl TangPhos (1)



To a solution of (*1R, 1R', 2R, 2R'*)-1, 1'-di-*tert*-butyl-[2,2']-diphospholanyl 1, 1'-disulfide (440 mg, 1.26 mmol) in 25ml benzene was added hexachlorodisilane (3.25 mL, 5.08 g, 18.9 mmol). The mixture was stirred at reflux for 4 h. After the solution was cooled to r.t., 50 mL of degassed 30% (w/w) NaOH solution was carefully added to the reaction mixture with an ice-water bath. The resulting mixture was then stirred at 60 °C until the aqueous layer became clear. The two phases were

separated. The water phase was washed twice with degassed benzene (2 x 30 mL). The combined benzene was dried over Na_2SO_4 and concentrated.

The solid residue was re-dissolved in a minimum amount of degassed dichloromethane, which was subsequently passed through a basic Al_2O_3 plug (eluent: Et_2O:hexane=1:10) to give pure white product **(1)** 320 mg (88% yield).

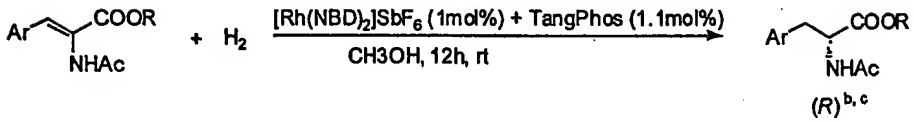
EXAMPLE 2: Asymmetric Hydrogenation of Dehydroamino Acids General Procedure for Asymmetric Hydrogenation.

To a solution of $[Rh(COD)_2]BF_4$ (5.0 mg, 0.012 mmol) in THF (10 mL) in a glovebox was added a chiral phosphine ligand (TangPhos 0.15 mL of 0.1 M solution in toluene, 0.015 mmol). After stirring the mixture for 30 min, the dehydroamino acid (1.2 mmol) was added. The hydrogenation was performed at rt under 20 psi of hydrogen for 24 h. The reaction mixture was treated with CH_2N_2, then concentrated in Vacuo. The residue was passed through a short silica gel column to remove the catalyst. The enantiomeric excesses were measured by GC using a Chirasil-VAL III FSOT column.

The absolute configuration of products was determined by comparing the observed rotation with the reported value. All reactions went in quantitative yield with no by-products found by GC.

Asymmetric hydorgenation for making alpha amino acid derivatives using TangPhos **(1)** as the ligand is shown in the Table below:

Asymmetric Hydrogenation of Dehydroamino Acid Derivatives[a]



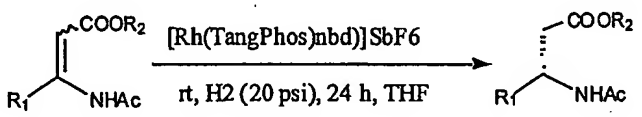
Entry	Substrate	ee[c] (%)
1	Ar = Ph, R = H	>99[d]
2	Ar = Ph, R =CH3	>99
3	Ar = p-F-Ph, R = H	99[d]
4	Ar = p-F-Ph, R = CH3	>99
5	Ar = p-MeO-Ph, R = H	>99[d,e]
6	Ar = p-MeO-Ph, R = CH3	>99
7	Ar = m-Br-Ph, R = H	>99[d]
8	Ar = m-Br-Ph, R = CH3	>99
9	Ar = o-Cl-Ph, R = H	>99[d]
10	Ar = o-Cl-Ph, R = CH3	>99
11	Ar = 2-thienyl, R = H	>99[d]
12	Ar = 2-thienyl, R = CH3	>99
13	Ar = 2-naphthyl, R = H	>99[d]
14	Ar = 2-naphthyl, R = CH3	>99
15	Ar = Ph, R = H, N-benzoyl	>99[d]
16	Ar = Ph, R = CH3, N-benzoyl	>99

[a] The reaction eas carried out at rt under 20psi of H_2 for 24h. THe catalyst was made in situ by sitirring a solution of $[Rh(NBD)_2]SbF_6$ and TangPhos in methanol (2mL) [substrate:[Rh]:TangPhos = 1:0.01:0.011]. The reaction went with 100% conversion. [b] The R absolute configuration was assigned by comparison of optical rotation with reported data. [c] Enantiomeric excesses were determined by chiral GC using a Chrialsil- VAL III FSOT column. [d] Determined on corresponding methyl ester. [e] The % ee was determined by HPLC using a Daicel Chiralcel OJ column.

EXAMPLE 3: Asymmetric Synthesis of Beta-Amino Acid Derivatives Synthesis of Starting Material 3-Acetamido-3-Aryl-2-Propenoates and 3-Acetamido-3-hetero-Aryl-2-Propenoates

Typical procedure: The starting material methyl 3-acetamido-3-phenyl-2-propenoate can be conveniently synthesized from cheap acetophenone in three steps according to known literature procedure in good yields. The literatures are Zhu, G.; Zhen, Z.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 6907-6910; Krapcho, A. P.; Diamanti, J. *Org. Synth.* **1973**, *5*, 198-201. ^{1}H-NMR ($CDCl_3$, 360 MHz) δ (Z isomer) 2.17 (s, 3H), 3.77 (s, 3H), 5.29 (s, 1H), 7.37-7.45 (m, 5H); (E isomer) 2.38 (s, 3H), 3.77 (s, 3H), 6.65 (s, 1H), 7.37-7.45 (m, 5H).

Hydrogenation for making beta amino acid derivatives with the Rh-TangPhos (1) system



entry[a]	R_1	R_2	geo m.[c]	ee[b] (%)	config.
1	Me	Et	*E*	99.5	*R*
2	Me	Et	*Z*	97.3	*R*
3	Me	*i*-Pr	*E*	99.3	*R*
4	Et	Me	*E*	99.6	*R*
5	*n*-Pr	Et	*E*	99.6	*R*
6	*i*-Bu	Me	*E*	98.5	*R*
7	Ph	Me	*E/Z*	93.8	*S*
8	*p*-F-Ph	Me	*E/Z*	95.0	*S*
9	*p*-Cl-Ph	Me	*E/Z*	92.3	*S*
10	*p*-Br-Ph	Me	*E/Z*	95.1	*S*
11	*p*-Me-Ph	Me	*E/Z*	94.0	*S*
12	*p*-MeO-Ph	Me	*E/Z*	98.5[d]	*S*
13	*p*-BnO-Ph	Me	*E/Z*	98.5	*S*
14	*o*-Me-Ph	Me	*E/Z*	74.3	*S*
15	*o*-MeO-Ph	Me	*E/Z*	83.1	*S*

[a] The reactions were carried out under 20 psi of H_2 in THF at rt for 24h. Substrate/[Rh(TangPhos)nbd]SbF_6 = 200:1. The absolute configurations were determined by comparing the optical rotations with reported values. [b] The ee (%) values were determined by chiral GC using a Chiralselect 1000 column. [c] For the *E*/*Z* ratios of *E*/*Z* mixtures. [d] The ee was determined by chiral HPLC using (*s*, *s*)-whelk-01 column

For general synthetic procedures of β-aryl β-acetamidoacrylate esters, see Zhou, Y.-G.; Tang, W.; Wang, W.-B.; Li, W.; Zhang, X. *J. Am. Chem. Soc.* **2002**, *124*, 4952-4953. For general synthetic procedure of β-alkyl β-acetamidoacrylate esters, see Zhu, G.; Chen, Z.; Zhang, X. *J. Org. Chem.* **1999**, *64*, 6907-6910. For analytical data of known substrates and products, please also refer to the two aforementioned papers.

Methyl 3-Acetamido-3-(4-benzyloxyphenyl)-2-propenoate:

Z/E = 9:1; ^{1}H NMR (360 MHz, $CDCl_3$) δ (*Z* isomer) 2.06 (s, 3H), 3.65 (s, 3H), 4.98 (s, 2H), 5.18 (s, 1H), 6.86 (d, *J* = 6.8 Hz, 2H), 7.28 (m, 7H), 10.46 (s, 1H); (E isomer) 2.27 (s, 3H), 3.65 (s, 3H), 4.98 (s, 2H), 6.44 (s, 1H), 6.86 (d, *J* = 6.8 Hz, 2H), 7.28 (m, 7H).

General procedure for asymmetric hydrogenation of β-alkyl or β-aryl β-acetamidoacrylic esters

To a solution of β-acetamidoacrylic ester (0.5 mmol) in 4 mL of degassed THF Rh[(TangPhos)nbd]SbF_6 (2.5 μmol) was added in a glovebox filled with nitrogen. The whole solution was transferred into an autoclave.

The autoclave was then purged three times with hydrogen and filled with hydrogen with 20 psi pressure. The resulting reactor was stirred at room temperature for 24 hr. After release of the hydrogen, the autoclave was opened and the reaction mixture was evaporated.

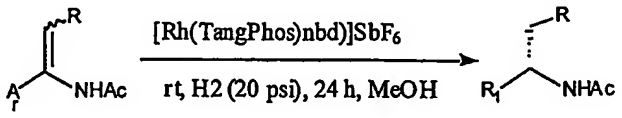
The residue was passed through a short silica gel plug to give hydrogenation product β-amino acid derivatives. A small amount of sample was subjected to chiral GC or HPLC analysis.

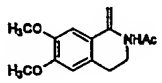
Methyl 3-acetamido-3-(4-benzyloxyphenyl)-propanoate:

98.5% ee, $[\alpha]^{25}_D$ = -79.5°; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.00 (s, 3H), 2.83 (dd, *J* = 15.7, 6.2 Hz, 1H), 2.93 (dd, *J* = 15.6, 6.0 Hz, 1H), 3.63 (s, 3H), 5.05 (s, 2H), 5.40 (m, 1H), 6.93 (d, 1H), 6.94 (dd, J = 6.7, 2.0 Hz, 2H), 7.23 (dd, J = 6.8, 1.8 Hz, 2H), 6.72 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.8, 40.2, 49.5, 52.2, 115.4, 127.9, 128.0, 128.4, 129.0, 133.3, 137.3, 158.6, 169.7, 172.1; MS (ESI) *m/z* 328 (M^++1); HRMS calculated for $C_{19}H_{22}NO_4$ 3281549, found 328.1553. Chiral HPLC conditions ((*s*, *s*)-whelk-01): solvent hexane:isopropanol(1:1); flow rate 1 mL/min; retention time 8.2 min (*R*), 13.1 min (*S*).

EXAMPLE 4: Asymmetric Hydrogenation of Enamides

Table. Rh-Catalyzed Asymmetric Hydrogenation of α-Arylenamides using TangPhos (1).

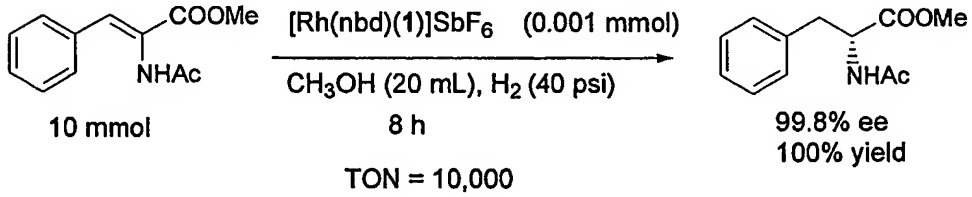


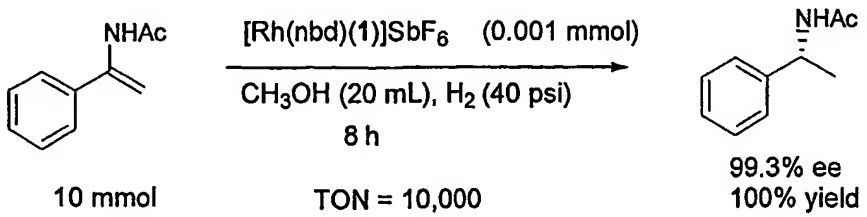
Entry	Substrate	Ar	R	ee [%][b]
1		Ph	H	>99
2		*m*-Me-Ph	H	>99
3		*p*-CF_3-Ph	H	>99
4		*p*-Cy-Ph	H	>99
5		*p*-Ph-Ph	H	99
6		2-naphthyl	H	>99
7		Ph	CH_3	98
8		*p*-CF_3-Ph	CH_3	98
9		*p*-MeO-Ph	CH_3	98
10		2-naphthyl	CH_3	99
11		Ph	$CH(CH_3)_2$	98
12		Ph	CH_2Ph	99
13				97

[a] Conditions: see Experimental Section for details. Enamides were prepared according to the literature method. [b] The *R* absolute configuration was assigned by comparison of optical rotation with reported data. ee's were determined by chiral GC using Supelco Chiral Select 1000 column or by chiral HPLC with a (*R*, *R*)-Poly Whelk-01 column.

Example 5: High turnovers for asymmetric hydrogenation of enamides using Rh(TangPhos (1) catalyst

Asymmetric hydrogenation with [Rh(NBD)TangPhos(1)]$^+SbF_6^-$ as the catalyst:

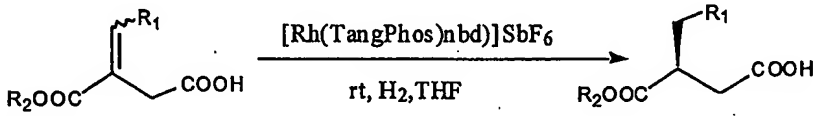




Procedure for hydrogenation of α-dehydro amino acid:

To a solution of methyl α-(acetylamino)-2-phenylacrylate (2.19 g, 10 mmol) in 20 mL of degassed methanol in glovebox was added [Rh(nbd)(1)]SbF_6 (1 ml of 0.001M solution in methanol, 0.001 mmol). The hydrogenation was performed at room temperature under 40 psi of H_2 for 8 h. After carefully releasing the hydrogen, the reaction mixture was passed through a short silica gel column to remove the catalyst. The enantiomeric excesses of (*R*)-methyl 2-acetylamino-3-phenylpropionate were measured by chiral GC directly. (Conversion: 100%, ee: 99.8%, TON: 10,000)

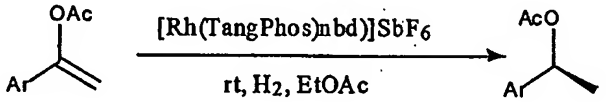
Example 6: Asymmetric hydrogenation of itaconic acid derivatives with Rh(TangPhos (1) catalyst



entry	R_1	R_2[b]	ee (%) [c]
1	H	H	99
2	CH_3	$CH(CH_3)_2$	96
3	CH_3	Ph	93
4	CH_3	*p*-MeO-Ph	97
5	CH_3	*p*-Me-Ph	97
6	CH_3	*p*-Cl-Ph	>99
7	CH_3	*m*-Cl-Ph	99
8	CH_3	1-naphthyl	99
9	CH_3	2-naphthyl	99

[a] Conditions: catalyst precursor = [Rh(TangPhos)(nbd)]SbF_6 (1 mol %), room temperature, 20 psi H_2, THF. The absolute configuration of product was determined by comparison with reported data. [b] Most substrates (except entry 1) employed as crude E/Z mixtures ranging from 2/1 to >10/1. [c] Determined on chiral GC or HPLC column after conversion of the hydrogenation product into dimethyl ester.

Example 7: Asymmetric hydrogenation of Arylenol Acetates with the [Rh(TangPhos (1)] catalyst



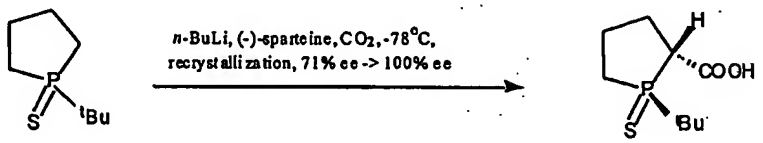
entry	Ar	ee (%) [b]
1	2-naphthyl	97
2	Ph	96
3	*p*-F-Ph	92
4	*p*-Cl-Ph	97
5	2-furyl	93
6	p-NO_2-Ph	99

[a] Conditions: catalyst precursor = [Rh(TangPhos)(nbd)]SbF_6 (1 mol %), room temperature, 20 psi H_2, EtOAc. The absolute configuration of product was determined by comparison with reported data. [b] Determined on a chiral GC column (chiral select 1000).

Example 8: Synthesis of Chiral PN ligands for asymmetric Catalysis

Since Ir-catalyzed asymmetric hydrogenation is still highly substrate-dependent, development of new efficient chiral ligands for Ir-catalyzed hydrogenation is a continuing challenge. A new class of chiral

P, N ligands, the phospholane-oxazolines have been developed as follows:



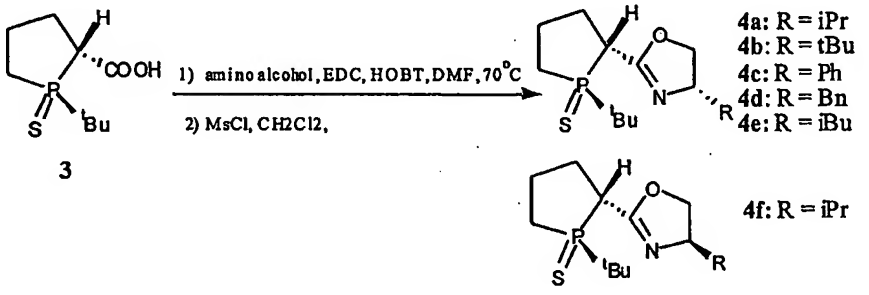
2 3

At -78°C, to a solution of (-)-sparteine (14.4 mL, 62.5 mmol) in ether (100 mL) was added dropwise n-BuLi (1.6M in hexane, 39 mL, 62.5 mmol). The mixture was stirred at -78°C for 30 min. A solution of **2** (10g, 56.8 mmol) in ether (150 mL) was added dropwise. The addition was complete in 1 h. The resulting reaction mixture was allowed to warm to rt and stirred overnight. The mixture was re-cooled to -78°C. Through the suspension was bubbled CO_2 for 2 h. Then it was quenched with the addition of 1N HCl (200 mL) followed by EtOAc (200 mL). The organic layer was washed sequentially with 1N HCl (200 mL), H_2O (200 mL), and brine (100 mL). The solution was dried over Na_2SO_4 and evaporated. The residue was treated with 2 N NaOH solution (300 mL). The resulting clear solution was neutralized by the addition of 2 N HCl. The precipitate was collected through vacuum filtration to give the product (8.0 g, 72% ee, 64% yield). The ee was determined by converting the product into its corresponding methyl ester by treatment with $TMSCHN_2$ in THF/CH_3OH solution (HPLC conditions for the methyl ester: Chiralpak AD column; hex:ipr = 95:5; 8.8 min, 11.3 min.) A sample of product (7.5 g) was recrystallized twice from ethanol to give 4.5 g of enantiomerically pure product **3** (>99.9% ee, 40% total yield).

3: $[\alpha]_D^{20}$ = 16.9° (c = 0.9, $CHCl_3$); ^1H NMR (360 MHz, $CDCl_3$) δ 1.35 (d, $^3J_{HP}$ = 17.0 Hz, 9H), 1.71 (m, 1H), 2.18 (m, 3H), 2.47 (m, 2H), 3.34 (m, 1H); ^{13}C NMR (90 MHz, CD_3OD) δ 25.4 (d, $^2J_{CP}$ = 1.7 Hz), 26.0 (d, $^2J_{CP}$ =

2.2 Hz), 31.3 (d, $^2J_{CP}$ = 7.3 Hz), 32.8 (d, J_{CP} = 48.8 Hz), 36.1 (d, J_{CP} = 44.1 Hz), 46.4 (d, J_{CP} = 36.0), 172.9; ^{31}P NMR (145 MHz, CD_3OD) δ 89.3 (s); APCI MS 121 (M^++H); HRMS calculated for $C_9H_{18}PSO_2$ 221.0765, found 221.0762.

The methyl ester of **3**: $[\alpha]_D^{20}$ = 42.6° (c = 1, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.21 (d, $^3J_{HP}$ = 16.8 Hz, 9H), 1.69 (m, 1H), 1.92 (m, 2H), 2.30 (m, 3H), 3.23 (m, 1H), 3.66 (s, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 25.2 (d, 2.7 Hz), 25.4 (d, $^2J_{CP}$ = 1.8 Hz), 29.9 (d, $^2J_{CP}$ = 7.4 Hz), 31.7 (d, J_{CP} = 47.9 Hz), 35.3 (d, J_{CP} = 43.5 Hz), 45.4 (d, J_{CP} = 35.5 Hz), 52.7, 170.0; ^{31}P NMR (145 MHz, $CDCl_3$) δ 87.8; APCI MS 235 (M^++H); HRMS calculated for $C_{10}H_{20}PSO_2$ 235.0922 found 235.0909.



A mixture of **3** (2.27 mmol), EDC.HCl (1.3 g, 6.82 mmol), HOBT.H_2O (0.52 g, 3.41 mmol), chiral amino alcohol (3.41 mmol), triethylamine (1.9 mL, 13.6 mmol) in 10 mL of DMF was stirred at 70°C overnight. To the cooled mixture was added 30 mL of 2 N HCl solution. The resulting mixture was then extracted with ethyl acetate. The organic layer was washed with water and brine, dried over Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography to give condensation product in 70-80% yield.

To a mixture of condensation product (1.67 mmol), diisopropylethylamine (1.98 mL, 6.68 mmol) and triethylamine (1.38 mL, 16.7 mmol) in 10 mL of CH_2Cl_2 was added 258 μL (3.34 mmol) of methanesulfonylchloride at 0°C. After addition, the resulting mixture was allowed to warm to room temperature and stirred overnight. The solvent was removed. The residue was redissolved in ethyl acetate, washed with water and brine, and dried over Na_2SO_4. After removal of solvent, the crude product was purified by column chromatography to give pure **4a-f** in 70-80% yield.

4a: $[\alpha]^{20}_D$ = -75.1° (c = 0.9, $CHCl_3$), ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.81 (d, 6.8 Hz, 3H), 0.89 (d, 6.8 Hz, 3H), 1.24 (d, $^3J_{HP}$ = 16.5 Hz, 9H), 1.58 (m, 1H), 1.71 (m, 1H), 1.90 (m, 1H), 2.11 (m, 2H), 2.37 (m, 2H), 3.19 (m, 1H), 3.86 (m, 1H), 3.94 (t, 7.9 Hz, 1H), 4.21 (t, 8.1 Hz, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 18.7, 19.4, 25.4 (m), 30.6 (d, $^2J_{CP}$ = 7.9 Hz), 31.8 (d, J_{CP} = 47.5 Hz), 32.0, 33.1, 35.2 (d, J_{CP} = 43.4 Hz), 38.8 (d, J_{CP} = 39.5 Hz), 70.6, 72.4, 163.9; ^{31}P NMR (145 MHz, $CDCl_3$) δ 88.0; APCI MS 288 (M^++H); HRMS calculated for $C_{14}H_{27}NOPS$ 288.1551 found 288.1549.

4b: $[\alpha]^{20}_D$ = -75.9° (c = 0.9, $CHCl_3$), ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.83 (s, 9H), 1.25 (d, $^3J_{HP}$ = 16.4 Hz, 9H), 1.56 (m, 1H), 1.87 (m, 1H), 2.14 (m, 2H), 2.38 (m, 2H), 3.21 (m, 1H), 3.83 (m, 1H), 4.01 (t, 8.4 Hz, 1H), 4.16 (t, 8.5 Hz, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 25.6 (d, $^2J_{CP}$ = 1.6 Hz), 26.5, 30.6 (d, $^2J_{CP}$ = 7.9 Hz), 31.9 (d, J_{CP} = 47.2 Hz), 32.0, 33.8, 35.3 (d, J_{CP} = 43.6 Hz), 38.9 (d, J_{CP} = 40.0 Hz), 69.1, 75.9, 163.9; ^{31}P NMR (145 MHz, $CDCl_3$) δ 87.3; ESI MS 302 (M^++H); HRMS calculated for $C_{15}H_{29}NOPS$ 302.1707 found 302.1716.

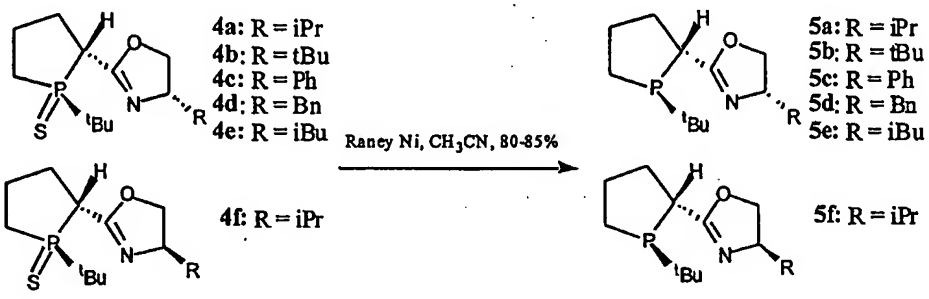
4c: $[\alpha]^{20}_D$ = -98.9° (c = 1, $CHCl_3$), ^1H NMR (360 MHz, $CDCl_3$) δ 1.24 (d, $^3J_{HP}$ = 16.6 Hz, 9H), 1.58 (m, 1H), 1.91 (m, 1H), 2.16 (m, 2H), 2.39 (m, 2H), 3.28 (m, 2H), 3.19 (t, 8.3 Hz, 1H), 4.58 (t, 8.3 Hz, 1H), 5.14 (m, 1H), 7.19 (m, 5H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 25.0 (d, $^2J_{CP}$ = 1.1 Hz), 30.2 (d, $^2J_{CP}$ = 7.7 Hz), 31.3 (d, J_{CP} = 47.3 Hz), 31.5, 34.8 (d, J_{CP} = 43.4 Hz), 38.6 (d, J_{CP} = 39.2 Hz), 69.6, 74.9, 127.3 (m), 142.3, 165.2 (d, $^2J_{CP}$ = 4.6 Hz); ^{31}P NMR (145 MHz, $CDCl_3$) δ 88.8; APCI MS 322 (M^++H); HRMS calculated for $C_{17}H_{25}NOPS$ 322.1395 found 322.1409.

4d: $[\alpha]^{20}_D$ = -54.2° (c = 1, $CHCl_3$), ^1H NMR (360 MHz, $CDCl_3$) δ 1.17 (d, $^3J_{HP}$ = 16.5 Hz, 9H), 1.52 (m, 1H), 1.84 (m, 1H), 2.07 (m, 2H), 2.32 (m, 2H), 2.58 (dd, 8.2 Hz, 13.6 Hz, 1H), 2.98 (dd, 5.5 Hz, 13.6 Hz,1H), 3.06 (dd, 9.6 Hz, 17.3 Hz, 1H), 3.88 (t, 7.3 Hz, 1H), 4.09 (t, 8.5 Hz), 4.3 (m, 1H), 7.13 (m, 5H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 24.4, 24.6 (d, $^2J_{CP}$ = 1.2 Hz), 29.8 (d, $^2J_{CP}$ = 8.0 Hz), 30.9 (d, J_{CP} = 47.4 Hz), 34.3 (d, J_{CP} = 43.4 Hz), 37.8 (d, J_{CP} = 39.1 Hz), 41.5, 66.8, 71.3, 125.8, 127.9, 128.8 (m), 163.7 (d, $^2J_{CP}$ = 4.7 Hz); ^{31}P NMR (145 MHz, $CDCl_3$) δ 88.5; APCI MS 336 (M^++H); HRMS calculated for $C_{18}H_{27}NOPS$ 336.1551 found 336.1542.

4e: $[\alpha]^{20}_D$ = -83.9° (c = 1, $CHCl_3$), ^1H NMR (360 MHz, $CDCl_3$) δ 0.67 (t, 6.4 Hz, 6H), 1.04 (d, $^3J_{HP}$ = 16.4 Hz, 9H), 1.43 (m, 3H), 1.67 (m, 1H), 1.94 (m, 2H), 2.19 (m, 2H), 3.00 (m, 1H), 3.60 (t, 7.4 Hz, 1H), 3.91 (m, 1H), 4.08 (m, 8.5 Hz, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 22.3, 22.5, 24.4, 24.6, 24.9, 29.8 (d, $^2J_{CP}$ = 7.9 Hz), 30.9 (d, J_{CP} = 47.4 Hz), 31.4 Hz, 34.3 (d, J_{CP} = 43.4 Hz), 37.9 (d, J_{CP} = 39.4 Hz), 45.3, 64.1, 72.6, 162.9 (d, $^2J_{CP}$ = 4.6 Hz); ^{31}P NMR (145 MHz, $CDCl_3$) δ 88.0; ESI MS 302 (M^++H); HRMS calculated for $C_{15}H_{28}NOPS$ 302.1708 found 302.1715.

4f: $[\alpha]^{20}_D$ = +28.6° (c = 0.9, $CHCl_3$), ^1H NMR (360 MHz, $CDCl_3$) δ 0.82 (d, 6.7 Hz, 3H), 0.94 (d, 6.7 Hz, 3H), 0.95 (d, $^3J_{HP}$ = 16.4 Hz, 9H),

1.58 (m, 1H), 1.75 (m, 1H), 1.89 (m, 1H), 2.13 (m, 2H), 2.39 (m, 2H), 3.11 (m, 1H), 3.81 (m, 1H), 3.95 (t, 8.2 Hz, 1H), 4.20 (t, 8.2 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ 18.6, 20.0, 25.2, 25.4 (d, $^2J_{CP}$ = 1.4 Hz), 30.7 (d, $^2J_{CP}$ = 7.8 Hz), 32.8 (d, J_{CP} = 47.6 Hz), 32.0, 33.2, 35.1 (d, J_{CP} = 43.6 Hz), 38.7 (d, J_{CP} = 39.8 Hz), 70.6, 72.8, 163.7 (d, $^2J_{CP}$ = 4.5 Hz); ^{31}P NMR (145 MHz, $CDCl_3$) δ 87.9; ESI MS 288 (M^++H); HRMS calculated for $C_{14}H_{27}NOPS$ 288.1551 found 288.1545.



General procedure:

To a N_2-flushed Schlenk flask was loaded 5.0 g of Raney Ni 2800 slurry. The Raney Ni was washed sequentially with methanol (10 mL x 3), ether (10 mL x 3), and dried degassed CH_3CN (10 mL x 3). To this flask was then transferred a solution of **4a-f** (1.5 mmol) in CH_3CN (20 mL) via cannula. The resulting mixture was stirred under N_2 for 2 d. The mixture was then filtered under N_2. The Raney Ni solid was washed with CH_3CN (10 mL x 5). The combined CH_3CN with filtrate was evaporated under N_2 to give an oily residue. The residue was passed through an Al_2O_3 (basic) plug under N_2 to give pure oily product **5a-f** (80-95%).

5a: ^1H NMR (400 MHz, CD_2Cl_2) δ 0.88 (d, 6.8 Hz, 3H), 0.94 (d, 6.8 Hz, 6.8 Hz), 1.08 (d, $^3J_{HP}$ = 11.9 Hz, 9H), 1.72 (m, 4H), 2.01 (b, 3H), 2.81 (b, 1H), 3.85 (b, 1H), 3.95 (t, 7.6 Hz, 1H), 4.20 (t, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 18.3, 18.8, 23.3 (d, $^2J_{CP}$ = 17.5 Hz), 27.6 (d, $^2J_{CP}$ =

14.5 Hz), 29.0, 29.1 (d, J_{CP} = 18.4 Hz), 33.2 (d, J_{CP} = 19.9 Hz), 36.9 (d, J_{CP} = 20.2 Hz), 70.2, 72.4, 169.1 (d, $^2J_{CP}$ = 15.9 Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ 26.0; ESI MS 256 (M^++H); HRMS calculated for $C_{14}H_{27}NOP$ 256.1830 found 256.1820.

5b: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.71 (s, 9H), 0.90 (d, $^3J_{HP}$ = 11.9 Hz, 9H), 1.56 (m, 3H), 1.83 (m, 3H), 2.73 (b, 1H), 3.65 (m), 3.92 (t, 7.6 Hz, 1H), 3.99 (t, 9.3 Hz, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 21.9 (d, $^2J_{CP}$ = 17.6 Hz), 24.8, 26.4 (d, $^2J_{CP}$ = 14.2 Hz), 27.7 (d, 2.84 Hz), 28.9 (d, J_{CP} = 18.0 Hz), 32.4 (d, J_{CP} = 70.0 Hz), 35.8 (d, J_{CP} = 19.8 Hz), 67.7, 74.4, 168.9 (d, , $^2J_{CP}$ = 15.9 Hz); ^{31}P NMR (145 MHz, $CDCl_3$) δ 25.2; ESI MS 270 (M^++H); HRMS calculated for $C_{15}H_{29}NOP$ 270.1987 found 270.1972.

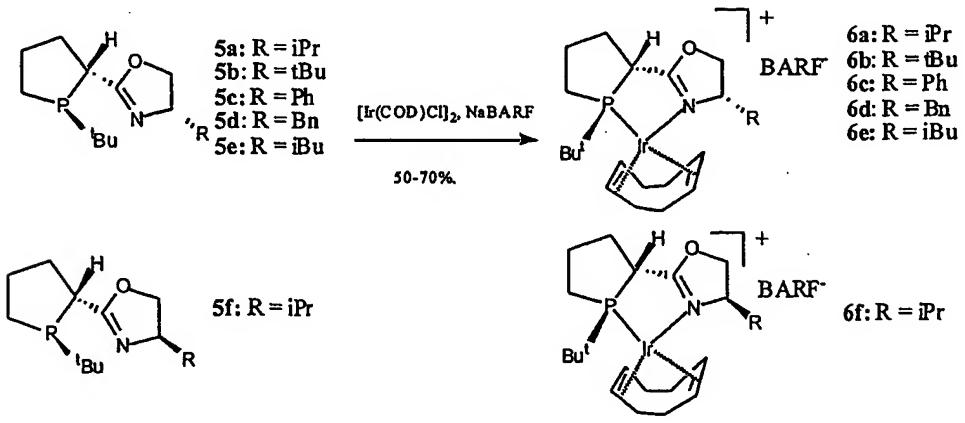
5c: ^{1}H NMR (360 MHz, CD_2Cl_2) δ 0.98 (d, $^3J_{HP}$ = 12.0 Hz, 9H), 1.66 (m, 3H), 1.92 (m, 3H), 2.80 (m, 1H), 3.91 (t, 7.9 Hz, 1H), 4.46 (dd, 8.3 Hz, 10.0 Hz, 1H), 5.01 (m, 1H), 7.17 (m, 5H); ^{13}C NMR (90 MHz, CD_2Cl_2) δ 23.5 (d, $^2J_{CP}$ = 17.6 Hz), 27.9 (d, $^2J_{CP}$ = 14.4 Hz), 29.2 (d, $^2J_{CP}$ = 2.1 Hz), 29.4 (d, J_{CP} = 18.7 Hz), 33.4, 37.1 (d, J_{CP} = 20.1 Hz), 70.1, 75.3, 127.0-129.1 (m), 144.0, 172.0 (d, $^2J_{CP}$ = 15.8 Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ 27.4; ESI MS 290 (M^++H); HRMS calculated for $C_{17}H_{24}NOP$ 290.1674 found 290.1663.

5d: ^{1}H NMR (360 MHz, CD_2Cl_2) δ 1.06 (d, $^3J_{HP}$ = 11.9 Hz, 9H), 1.74 (m, 3H), 2.01 (m, 3H), 2.67 (dd, 7.5 Hz, 13.6 Hz, 1H), 2.74 (m, 1H), 2.96 (dd, 6.1 Hz, 13.6 Hz, 1H), 3.92 (dd, 7.0 Hz, 8.2 Hz, 1H), 4.17 (t, 9.0 Hz, 1H), 4.30 (m, 1H), 7.28 (m, 5H); ^{13}C NMR (90 MHz, CD_2Cl_2) δ 23.4 (d, J_{CP} = 17.9 Hz), 27.8 (d, $^2J_{CP}$ = 14.4 Hz), 29.1 (d, $^2J_{CP}$ = 2.2 Hz), 29.3 (d, J_{CP} = 18.7 Hz), 33.4 (d, $^2J_{CP}$ = 1.2 Hz), 37.1 (d, J_{CP} = 20.0 Hz), 42.5, 68.0, 72.2, 126.8, 128.9, 130.0, 139.2, 170.9 (d, $^2J_{CP}$ = 15.8 Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ 26.7; ESI MS 304 (M^++H); HRMS calculated for $C_{18}H_{27}NOP$ 304.1830 found 304.1836.

5e: ^{1}H NMR (360 MHz, CD_2Cl_2) δ 0.86 (d, 4.3 Hz, 3H), 0.92 (d, 4.3 Hz, 3H), 1.03 (d, $^3J_{HP}$ = 11.9 Hz, 9H), 1.25 (m, 1H), 1.49 (m, 1H), 1.73 (m, 4H), 1.95 (m, 3H), 2.74 (m, 1H), 3.75 (t, 7.7 Hz, 1H), 4.03 (m, 1H), 4.25 (dd, 8.0 Hz, 9.1 Hz, 1H); ^{13}C NMR (90 MHz, CD_2Cl_2) δ 23.1, 23.3 (d, $^2J_{CP}$ = 17.7 Hz), 26.0, 27.8 (d, $^2J_{CP}$ = 14.4 Hz), 29.1 (d, $^2J_{CP}$ = 2.4 Hz), 29.2 (d, J_{CP} = 18.7 Hz), 33.3 (d, 1.6 Hz), 37.1 (d, J_{CP} = 19.9 Hz), 46.3, 65.2, 73.4, 169.9 (d, $^2J_{CP}$ = 15.8 Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ 26.1; ESI MS 270 (M^++H); HRMS calculated for $C_{15}H_{28}NOP$ 270.1987 found 270.2042.

5f: ^{1}H NMR (360 MHz, $CDCl_3$) δ 0.73 (d, 6.8 Hz, 3H), 0.80 (d, 6.8 Hz, 3H), 0.93 (d, $^3J_{HP}$ = 12.0 Hz, 9H), 1.49 (m, 1H), 1.66 (m, 3H), 1.89 (m, 3H), 2.66 (m, 1H), 3.76 (m, 1H), 3.84 (t, 7.6 Hz, 1H), 4.07 (t, 8.8 Hz, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 16.6, 17.9, 21.8 (d, $^2J_{CP}$ = 17.4 Hz), 26.5 (d, $^2J_{CP}$ = 14.3 Hz), 27.5 (d, $^2J_{CP}$ = 2.4 Hz), 27.8 (d, J_{CP} = 18.0 Hz), 31.3, 31.9 (d, 1.1 Hz), 35.5 (d, J_{CP} = 19.8 Hz), 68.5, 70.6, 169.0 (d, $^2J_{CP}$ = 15.5 Hz); ^{31}P NMR (145 MHz, $CDCl_3$) δ 25.9; ESI MS 256 (M^++H); HRMS calculated for $C_{14}H_{27}NOP$ 256.1830 found 256.1805.

Example 9 , Preparation of Ir-PN Compounds



General procedure:

To a Schlenk tube was added **5a-f** (0.346 mmol), $[Ir(COD)Cl]_2$ (116 mg, 0.173 mmol), and dried degassed CH_2Cl_2 (4 mL). The deep red mixture was heated under N_2 to reflux for 1 h, until in situ ^{31}P NMR indicated that the starting material was consumed. After the reaction mixture was cooled to rt, Na[BARF] (453 mg, 0.519 mmol) was added followed by degassed H_2O (5 mL), and the resulting two-phase mixture was stirred vigorously for 30 min. The two layers were separated, and the water layer was further washed with CH_2Cl_2. The combined CH_2Cl_2 solution was evaporated to give a brown residue, which was subsequently passed through an Al_2O_3 plug (eluent: hexane: CH_2Cl_2 = 1 : 2) to give pure orange product **6a-f** in 50-70% yield.

6a: ^1H NMR (360 MHz, CD_2Cl_2) δ 0.74 (d, 6.8 Hz, 3H), 0.91 (d, 7.0 Hz, 3H), 1.17 (d, $^3J_{HP}$ = 15.4 Hz, 9H), 1.58 (m, 2H), 1.83-2.40 (m, 13H), 3.09 (m, 1H), 4.13 (m, 3H), 4.51 (t, 9.4 Hz, 1H), 4.65 (dd, 3.8 Hz, 9.4 Hz, 1H), 4.94 (m, 2H), 7.59 (s, 4H), 7.73 (s, 8H); ^{13}C NMR (90 MHz, CD_2Cl_2) δ 14.0, 19.0, 24.0 (d, $^2J_{CP}$ = 25.6 Hz), 27.1 (d, $^2J_{CP}$ = 3.5Hz), 27.8, 30.1 (d, 1.9 Hz), 31.1, 32.2 (d, 1.9 Hz), 32.5 (d, J_{CP} = 23.4 Hz), 33.9 (d, 2.1 Hz), 36.2 (d, 3.7 Hz), 37.8 (d, J_{CP} = 30.0 Hz), 60.6, 63.1, 70.0, 73.0, 90.3 (d, 11.8 Hz), 93.5 (d, 10.9 Hz), 118.0 (t), 120.7, 123.7, 126.7, 129.3 (dd, 28.4 Hz, 58.6 Hz), 135.4 (t, 92.9 Hz), 162.3 (q, 49.6 Hz), 190.1 (d, $^2J_{CP}$ = 19.7 Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ 51.9; ESI+ MS: 556 (cation + 1); ESI- MS: 863 (anion); HRMS calculated for $IrC_{22}H_{39}NOP$ 556.2320 found 556.2318; HRMS calculated for $C_{32}H_{12}F_{24}B$ 863.0649 found 863.0650.

6b: ^1H NMR (360 MHz, CD_2Cl_2) δ 0.88 (s, 9H), 1.15 (d, $^3J_{HP}$ = 15.4 Hz, 9H), 1.43 (b, 2H), 1.60-2.40 (m, 11H), 2.87 (d, 7.6 Hz, 1H), 3.55 (m, 1H), 3.80 (b, 1H), 4.38 (m, 2H), 4.54 (m, 1H), 4.73 (dd, 1.8 Hz, 9.8 Hz), 5.02 (b, 1H), 7.48 (s, 4H), 7.64 (s, 8H); ^{13}C NMR (90 MHz, CD_2Cl_2) δ 23.7, 24.0, 25.5, 26.0, 25.5, 27.3 (d, $^2J_{CP}$ = 3.4 Hz), 29.4, 31.5 (d, J_{CP} = 25.5

Hz), 34.0, 34.8, 35.7, 37.2 (d, J_{CP} = 30.3 Hz), 37.7, 56.5, 65.2, 71.1, 75.2, 86.0 (d, 16.5 Hz), 96.0 (d, 8.1 Hz), 111.8 (t), 120.7, 123.7, 126.7, 129.4 (dd, 28.5 Hz, 62.7 Hz), 135.4 (t), 162.3 (q, 49.4 Hz), 188.4 (d, $^2J_{CP}$ = 17.9 Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ 42.4; ESI+ MS: 570 (cation + 1); HRMS calculated for $IrC_{23}H_{41}NOP$ 570.2477 found 570.2437; HRMS calculated for $C_{32}H_{12}F_{24}B$ 863.0649 found 863.0633.

6c: ^{1}H NMR (360 MHz, CD_2Cl_2) δ 1.09 (d, $^3J_{HP}$ = 15.5 Hz, 9H), 1.25 (m, 1H), 1.46 (m, 2H), 1.80-2.40 (m, 11H), 3.19 (m, 1H), 3.78 (m, 2H), 4.00 (m, 1H), 4.46 (dd, 5.2 Hz, 9.2 Hz, 1H), 4.81 (m, 1H), 4.93 (dd, 9.4 Hz, 10.0 Hz, 1H), 5.23 (m, 1H), 7.01 (m, 2H), 7.34 (m, 3H), 7.48 (s, 4H), 6.65 (s, 8H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 23.1 (d, $^2J_{CP}$ = 26.5 Hz), 27.3, 27.6, 28.0, 28.5, 30.9, 31.4, 33.0 (d, J_{CP} = 23.6 Hz), 33.9, 35.4, 37.1 (d, J_{CP} = 29.9 Hz), 61.7, 62.6, 69.4, 81.3, 93.3 (d, 11.6 Hz), 94.2 (d, 13.9 Hz), 118.3, 121.3, 124.0, 126.5, 126.7, 129.6 (dd, 25.2 Hz, 67.1 Hz), 130.5 (m), 135.6, 139.2, 162.5 (q, 49.5 Hz), 191.3 (d, $^2J_{CP}$ = 19.8 Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ 53.7; ESI+ MS: 590 (cation + 1); HRMS calculated for $IrC_{25}H37NOP$ 590.2164 found 570.2120.

6d: ^{1}H NMR (360 MHz, CD_2Cl_2) δ 1.18 (d, $^3J_{HP}$ = 15.5 Hz, 9H), 1.64 (m, 3H), 1.80-2.50 (m, 11H), 2.61 (dd, 9.8 Hz, 14.1 Hz, 1H), 3.06 (m, 2H), 4.08 (m, 1H), 4.29 (m, 2H), 4.49 (t, 9.0 Hz, 1H), 4.69 (dd, 2.7 Hz, 9.4 Hz), 4.98 (m, 1H), 5.12 (b, 1H), 7.20 (m, 2H), 7.35 (m, 3H), 7.57 (s, 4H), 7.73 (s, 8H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 23.7 (d, $^2J_{CP}$ = 24.6 Hz), 26.6, 27.0 (d, $^2J_{CP}$ = 3.7 Hz), 27.2, 30.0 (d, J_{CP} = 15.4 Hz), 32.1, 32.3 (d, 6.3 Hz), 33.4, 36.3 (d, 3.7 Hz), 36.7 (d, J_{CP} = 30.1 Hz), 41.4, 60.4, 64.0, 65.2, 76.6, 88.9 (d, 12.6 Hz), 94.3 (d, 10.3 Hz), 117.8, 120.9, 123.6, 126.3, 128.3, 129.1 (m), 129.6, 134.5, 135.2, 162.0 (q, 49.5 Hz), 190.1 (d, $^2J_{CP}$ = 19.2 Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ 52.0; ESI+ MS: 604 (cation + 1); HRMS calculated for $IrC_{26}H39NOP$ 604.2320 found 604.2322.

6e: ^{1}H NMR (360 MHz, CD_2Cl_2) δ 0.93 (d, 6.5 Hz, 3H), 0.97 (d, 6.5 Hz), 1.18 (d, $^3J_{HP}$ = 15.5 Hz, 9H), 1.39 (m, 2H), 1.60 (m, 4H), 1.80-2.50 (m, 11H), 3.06 (d, 7.6 Hz), 3.98 (m, 2H), 4.21 (m, 1H), 4.56 (m, 2H), 4.77 (m, 1H), 5.01 (m, 1H), 7.57 (s, 4H), 7.73 (s, 8H); ^{13}C NMR (90 MHz, CD_2Cl_2) δ 21.6, 23.8, 23.9 (d, $^2J_{CP}$ = 24.6 Hz), 25.8, 26.5, 27.1 (d, $^2J_{CP}$ = 3.7 Hz), 27.4, 30.2, 32.3 (d, J_{CP} = 24.1 Hz), 32.5, 33.8, 36.4 (d, 3.8 Hz), 37.0 (d, J_{CP} = 30.2 Hz), 45.0, 60.4, 63.3, 64.0, 77.6, 89.2 (d, 12.4 Hz), 64.6 (d, 40.9 Hz), 118.1 (t), 120.7, 123.7, 126.7, 129.5 (dd, 37.7 Hz, 76.2 Hz), 135.4 (t, 103.7 Hz), 162.4 (q, 49.7 Hz), 189,5 (d, $^2J_{CP}$ = 24.6 Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ 51.3; ESI+ MS: 570 (cation + 1); HRMS calculated for $IrC_{23}H_{41}NOP$ 570.2477 found 570.2423.

6f: ^{1}H NMR (400 MHz, CD_2Cl_2) δ 0.79 (d, 6.8 Hz, 3H), 1.00 (d, 7.1 Hz, 3H), 1.18 (d, $^3J_{HP}$ = 15.5 Hz, 9H), 1.80-2.30 (m, 12H), 2.40 (m, 2H), 3.55 (m, 1H), 4.18 (m, 1H), 3.93 (m, 1H), 4.46 (m, 1H), 4.52 (t, 9.4 Hz, 1H), 4.58 (m, 1H), 4.75 (dd, 3.6 Hz, 9.7 Hz, 1H), 5.02 (m, 1H), 7.61 (s, 4H), 7.77 (s, 8H); ^{13}C NMR (100 MHz, CD_2Cl_2) δ 14.3 (d, 9.6 Hz), 18.6 (d, 3.5 Hz), 22.6 (d, $^2J_{CP}$ = 29.7 Hz), 27.1 (d, $^2J_{CP}$ = 4.6 Hz), 27.6, 27.7, 31.5, 31.8, 32.5, 33.5 (d, J_{CP} = 21.2 Hz), 35.1, 36.4 (d, J_{CP} = 30.4 Hz), 62.5 (d, 7.5 Hz), 65.4, 68.9, 73.3, 85.6 (d, 14.2 Hz), 94.9 (d, 8.7 Hz), 117.7, 120.9, 123.6, 126.3, 129.2 (dd, 37.2 Hz, 68.5 Hz), 135.2, 162.1 (q, 49.7 Hz), 187.0 (d, $^2J_{CP}$ = 20.9 Hz); ^{31}P NMR (145 MHz, CD_2Cl_2) δ 60.0; ESI+ MS: 556 (cation + 1); ESI- MS: 863 (anion); HRMS calculated for $IrC_{22}H_{39}NOP$ 556.2320 found 556.2309; HRMS calculated for $C_{32}H_{12}F_{24}B$ 863.0649 found 863.0650.

Example 10: Asymmetric Reduction of Unfunctionalized Alkenes

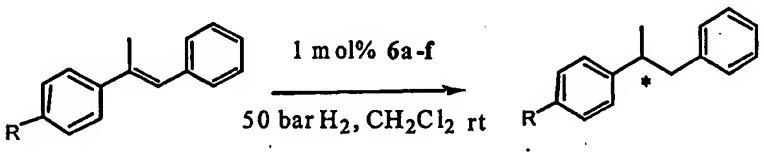
General hydrogenation procedure:

To a solution of an olefin substrate (0.2 mmol) in CH_2Cl_2 (2 mL) was added Ir complex **6** (2 μmol, 1 mol %) under nitrogen. The solution

was then transferred into an autoclave. The hydrogenation was performed at room temperature under 50 bar of H_2 for 12-48 h. After carefully releasing the hydrogen, the reaction mixture was evaporated. The residue was re-dissolved with ethyl acetate, which was subsequently passed through a short silica gel plug to remove the catalyst.

The resulting solution was directly used for chiral GC or HPLC to measure the enantiomeric excess.

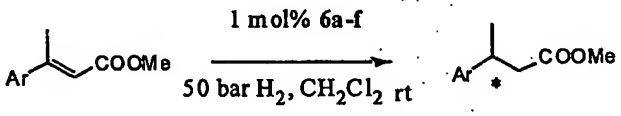
Ir-catalyzed asymmetric hydrogenation of methylstilbenes



Entry[a]	Substrate	R	Catalyst	ee % [b]	Config.[c]
1		H	**6a**	91	R
2		H	**6b**	81	R
3		H	**6c**	95	R
4		H	**6d**	89	R
5		H	**6e**	75	R
6		H	**6f**	77	S
7		OMe	**6c**	91	R
8		Cl	**6c**	90	R

[a] See Experimental Section for detailed conditions. [b] ee's were determined by Chiral HPLC (Chiralcel OJH). [c]The absolute configuration was assigned by comparison of optical rotation with reported data.

Ir-catalyzed asymmetric hydrogenation of β-methylcinnamic esters



Entry[a]	Substrate	R	Catalyst	ee %[b]	Config.[c]
1	**7**	Ph	**6a**	94	*R*
2	**7**	Ph	**6b**	91	*R*
3	**7**	Ph	**6c**	98	*R*
4	**7**	Ph	**6d**	92	*R*
5	**7**	Ph	**6e**	95	*R*
6	**7**	Ph	**6f**	93	*S*
7	**8**	*p*-F-Ph	**6c**	95	*R*
8	**9**	*p*-Cl-Ph	**6c**	98	*R*
9	**10**	*p*-CH_3-Ph	**6c**	97	*R*
10	**11**	*p*-OCF_3-Ph	**6c**	97	*R*
11	**12**	*p*-OCH_3-Ph	**6c**	97	*R*
12	**13**	*m*-CH_3-Ph	**6c**	99	*R*
13	**14**	1-naphthyl	**6c**	98	*R*
14	**15**	2-naphthyl	**6c**	95	*R*
15	(Z)-**9**	*p*-Cl-Ph	**6c**	80	*S*

[a] See Experimetal Section for detailed conditions. [b] ee's were determined by chiral HPLC (Chiralcel OJH) or Chiral GC (Chiralselect 1000). [c]The absolute configuration was assigned by comparison of optical rotation with reported data or by analogy.

A series of (*E*)-α,β-unsaturated esters were prepared via a Heck reaction according to a known procedure: Littke, A. F.; Fu, G. C. *J. Am. Chem. Soc.*, **2001**, *123*, 6989 -7000. To a Schlenk flask was added aryl halide (6.6 mmol), methyl crotonate (1.40 mL, 13.2 mmol), $Pd_2(dba)_2$ (151 mg, 165 μmol), Cy_2NMe (1.55 mL, 7.26 mmol), degassed dried dioxane (20 mL), and then $^tBu_3P$ (67 mg, 0.33 mmol). The whole mixture was stirred under N_2 at rt overnight. At the conclusion of the reaction, the mixture was diluted with Et_2O, filtered through a pad of silica gel with copious washing, concentrated, and purified through column chromatography to give product in 70-80% yield.

7: ^1H NMR (300 MHz, $CDCl_3$) δ 2.62 (d, 1.3 Hz, 3H), 3.78 (s, 3H), 6.17 (d, 1.2 Hz, 1H), 7.40 (m, 3H), 7.51 (m, 2H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 18.4, 51.5, 117.1, 126.7, 128.9, 129.5, 142.6, 156.3, 167.7; APCI MS: 177 (M^++1); HRMS calculated for $C_{11}H_{13}O_2$ 177.0916 found 177.0906.

8: ^1H NMR (360 MHz, $CDCl_3$) δ 2.55 (d, 1.2 Hz, 3H), 3.74 (s, 3H), 6.09 (d, 1.2 Hz, 1H), 7.05 (m, 2H), 7.45 (m, 2H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 18.2, 51.3, 115.6 (d, 21.6 Hz), 116.8, 128.8 (d, 32.0 Hz), 138.4, 154.7, 162.1, 164.8, 167.3; APCI MS: 195 (M^++1); HRMS calculated for $C_{11}H_{12}O_2F$ 195.0821 found 195.0824.

9: ^1H NMR (300 MHz, $CDCl_3$) δ 2.58 (d, 1.3 Hz, 3H), 3.78 (s, 3H), 6.14 (dd, 1.2 Hz, 2.4 Hz, 1H), 7.38 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3, 51.6, 117.5, 128.0, 129.1, 135.5, 140.9, 154.8, 167.5; APCI MS: 211 (M^++1); HRMS calculated for $C_{11}H_{12}O_2Cl$ 211.0526 found 211.0519.

10: ^1H NMR (300 MHz, $CDCl_3$) δ 2.40 (s, 3H), 2.61 (d, 1.2 Hz, 3H), 3.79 (s, 3H), 6.17 (d, 1.2 Hz, 1H), 7.21 (d, 8.0 Hz, 2H), 7.42 (d, 8.0 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.3, 21.6, 51.5, 116.2, 126.7, 129.6,

139.6, 156.2, 167.8; APCI MS: 191 (M^++1); HRMS calculated for $C_{12}H_{15}O_2$ 191.1072 found 191.1058.

11: ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.59 (d, 1.2 Hz, 3H), 3.79 (s, 3H), 6.15 (d, 1.2 Hz, 1H), 7.24 (d, 8.1 Hz, 2H), 2.55 (dd, 2.0 Hz, 7.9 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ 18.1, 51.3, 117.7, 119.2, 121.0, 121.1, 128.0, 140.9, 149.9, 154.3, 167.1;

12: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.58 (d, 1.2 Hz, 3H), 3.74 (s, 3H), 3.81 (s, 3H), 6.13 (dd, 1.1 Hz, 2.4 Hz, 1H), 6.89 (dd, 2.1 Hz, 6.8 Hz, 2H), 7.45 (dd, 2.1 Hz, 6.8 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.0, 51.4, 55.7, 114.2, 115.2, 134.5, 155.6, 160.9, 167.8; APCI MS: 207 (M^++1); HRMS calculated for $C_{12}H_{15}O_3$ 207.1021 found 207.1023.

13: ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.40 (s, 3H), 2.60 (d, 1.0 Hz, 3H), 3.78 (s, 3H), 6.16 (d, 1.0 Hz, 1H), 7.21 (m, 1H), 7.29 (m, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 18.2, 21.6, 51.2, 116.8, 123.6, 127.2, 128.6, 130.0, 138.3, 142.4, 156.3, 167.5; ESI MS: 191 (M^++1); HRMS calculated for $C_{12}H_{15}O_2$ 191.1072 found 191.1091.

14: ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.68 (s, 3H), 3.83 (s, 3H), 6.04 (s, 1H), 7.32 (m, 1H), 7.53 (m, 3H), 7.90 (m, 3H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 21.9, 51.3, 120.4, 124.4, 125.4, 126.2, 126.5, 128.4, 128.7, 130.3, 133.9, 142.2, 157.6, 167.2; ESI MS: 227 (M^++1); HRMS calculated for $C_{15}H_{15}O_2$ 227.1072 found 227.1066.

15: ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.74 (s, 3H), 3.82 (s, 3H), 6.33 (s, 1H), 7.56 (m, 3H), 7.90 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.4, 51.6, 117.5, 124.4, 126.4, 127.0, 127.2, 128.0, 128.6, 128.9, 133.5, 133.9, 139.6, 156.1, 167.7; APCI MS: 227 (M^++1); HRMS calculated for $C_{15}H_{15}O_2$ 227.1072 found 227.1064.

Analytical data and GC or HPLC conditions for new hydrogenation products

Hydrogenation Product of **7**:

98% ee; $[\alpha]^{20}_D$ = -15.5° (c = 0.7, $CHCl_3$); chiral HPLC: Chiralcel OJH, hex: *i*Pr = 95: 5, t_R = 7.9 min (*R*), 9.0 min (*S*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (d, 7.0 Hz, 3H), 2.58 (dd, 8.2 Hz, 15.1 Hz, 1H), 2.66 (dd, 6.9 Hz, 15.1 Hz, 1H), 3.30 (s, 3H), 7.31 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 36.9, 43.2, 51.9, 126.8, 127.1, 128.9, 146.1, 173.3; APCI MS: 196 (M^++NH_4^+); HRMS calculated for $C_{11}H_{18}NO_2$ 196.1338 found 196.1335.

Hydrogenation product of **8**:

95% ee; $[\alpha]^{20}_D$ = -1.9° (c = 0.5, $CHCl_3$); chiral GC: Chiralselect 1000, 140°C, t_R = 19.3 min (*S*), 19.9 (*R*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (d, 7.0 Hz, 3H), 2.60 (m, 2H), 3.30 (m, 1H), 3.64 (s, 3H), 7.16 (d, 8.0 Hz, 2H), 7.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 36.2, 43.0, 51.9, 121.4, 128.4, 144.7, 148.1, 172.9; APCI MS: 214 (M^++NH_4^+); HRMS calculated for $C_{11}H_{17}FNO_2$ 214.1243 found 214.1248.

Hydrogenation product of **9**:

98% ee; $[\alpha]^{20}_D$ = -32.4° (c = 1.1, $CHCl_3$); chiral GC: Chiralselect 1000, 140°C, t_R = 53.7 min (*S*), 55.5 min (*R*); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.29 (d, 7.0 Hz, 3H), 2.58 (m, 2H), 3.29 (m, 1H), 3.63 (s, 3H), 7.17 (m, 2H), 7.27 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 36.3, 43.0, 52.0, 128.5, 129.0, 132.4, 144.5, 173.0; APCI MS: 230 (M^++NH_4^+); HRMS calculated for $C_{11}H_{17}ClNO_2$ 230.0948 found 230.0942.

Hydorgenation product of **10**:

97% ee; $[\alpha]^{20}_D$ = -2.4° (c = 0.3, $CHCl_3$); chiral GC: Chiralselect 1000, 140°C, t_R = 27.1 min (*S*), 27.7 min (*R*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.31 (d, 7.0 Hz, 3H), 2.35 (s,3H), 2.56 (dd, 8.2 Hz, 15.1 Hz, 1H), 2.64 (dd, 7.0 Hz, 15.1 Hz, 1H), 3.29 (m, 1H), 3.66 (s, 3H), 7.14 (s, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 22.3, 36.4, 43.2, 51.9, 127.0, 129.6, 136.3, 143.1, 173.3; ESI MS: 210 (M^++NH_4^+); HRMS calculated for $C_{12}H_{20}NO_2$ 210.1494 found 210.1479.

Hydrogenation product of **11**:

97% ee; $[\alpha]^{20}_D$ = -23.4° (c = 0.3, $CHCl_3$); chiral GC: Chiralselect 1000, 140°C, t_R = 20.0 min (*S*), 20.5 min (*R*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (d, 7.0 Hz, 3H), 2.58 (m, 2H), 3.29 (m, 1H), 3.66 (s, 3H), 6.99 (m, 2H), 7.20 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.4, 36.2, 43.2, 51.9, 115.5, 128.5, 141.7, 160.6, 163.1, 173.1; ESI MS: 280 (M^++NH_4^+); HRMS calculated for $C_{12}H_{17}F_3NO_3$ 280.1161 found 280.1173.

Hydrogenation product of **12**:

97% ee; $[\alpha]^{20}_D$ = -23.8° (c = 0.7, $CHCl_3$); chiral HPLC: Chiralcel OJH, hex: *i*Pr = 95: 5, t_R = 12.1 min (*R*), 13.9 min (*S*); ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.27 (d, 7.5 Hz, 3H), 2.52 (dd, 8.0 Hz, 15.0 Hz, 1H), 2.59 (dd, 7.1 Hz, 15.0 Hz, 1H), 3.61 (s, 3H), 3.78 (s, 3H), 6.83 (m, 2H), 7.15 (m, 2H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 22.1, 35.9, 43.2, 51.6, 55.4, 114.1, 127.8, 138.1, 158.3, 173.1; ESI MS: 226 (M^++NH_4^+); HRMS calculated for $C_{12}H_{20}NO_3$ 226.1443 found 226.1425.

Hydrogenation product of **13**:

99% ee; $[\alpha]^{20}_D$ = -20.2° (c = 0.5, $CHCl_3$); chiral GC: Chiralselect 1000, 140°C, t_R = 47.0 min (*S*), 48.0 min (*R*); ^{1}H NMR (360 MHz, $CDCl_3$) δ 1.31 (d, 7.0 Hz, 3H), 2.35 (s, 3H), 2.52 (dd, 8.4 Hz, 15.2 Hz, 1H), 2.64 (dd, 6.7 Hz, 15.1 Hz, 1H), 3.25 (m, 1H), 3.65 (s, 3H), 7.04 (m, 3H), 7.21 (m,

1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 21.6, 22.0, 35.5, 36.5, 42.9, 51.6, 123.9, 127.4, 127.7, 128.6, 138.2, 145.9, 173.1; ESI MS: 210 (M^++NH_4^+); HRMS calculated for $C_{12}H_{20}NO_2$ 210.1494 found 210.1479.

Hydrogenation product of **14**:

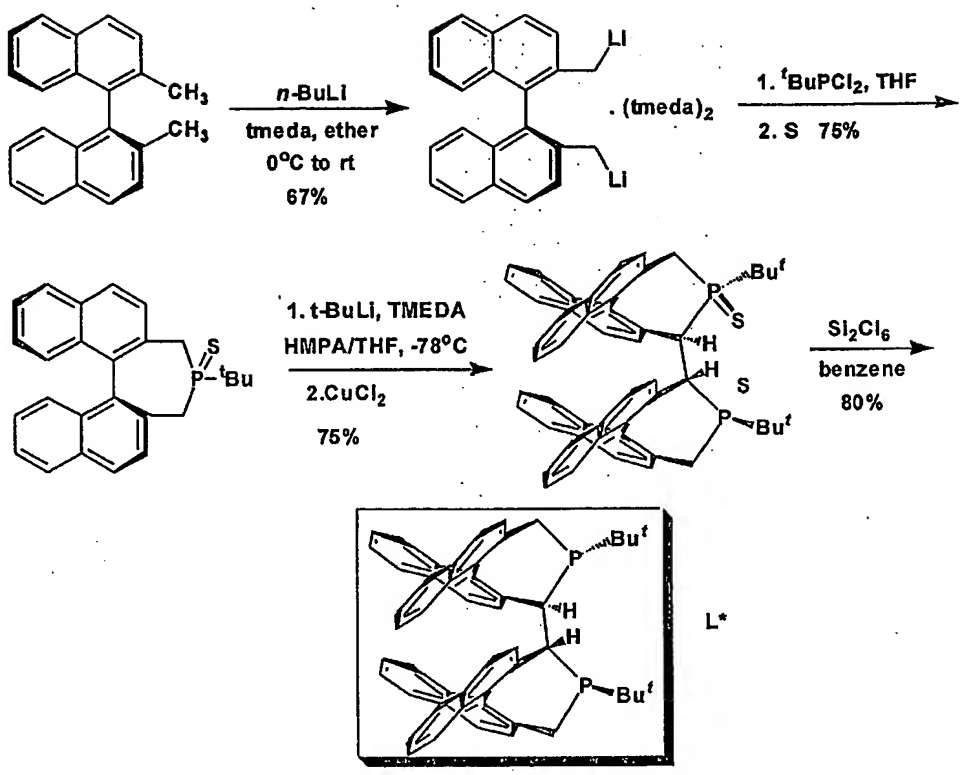
98% ee; $[\alpha]^{20}_D$ = +1.8° (c = 0.72, $CHCl_3$); chiral HPLC: Chiralcel OJH, hex: *i*Pr = 99:1, t_R = 32.2 min (*R*), 36.5 min (*S*); ^1H NMR (400 MHz, $CDCl_3$) δ 1.48 (d, 6.9 Hz, 3H), 2.67 (dd, 9.3 Hz, 15.3 Hz, 1H), 2.89 (dd, 5.3 Hz, 15.3 Hz, 1H), 3.70 (s, 3H), 4.21 (m, 1H), 7.50 (m, 4H), 7.77 (d, 8.0 Hz, 1H), 7.90 (d, 8.0 Hz, 1H), 8.22 (d, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 31.2, 42.7, 51.9, 122.7, 123.4, 125.9, 126.5, 127.4, 129.4, 131.5, 134.4, 142.1, 173.5; ESI MS: 246 (M^++NH_4^+); HRMS calculated for $C_{15}H_{20}NO_2$ 246.1494 found 246.1497.

Hydrogenation product of **15**:

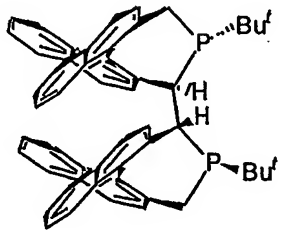
95% ee; $[\alpha]^{20}_D$ = -40.2° (c = 1.2, $CHCl_3$); chiral HPLC: Chiralcel OJH, hex: *i*Pr = 99:1, t_R = 65.2 min (*R*), 70.9 min (*S*); ^1H NMR (300 MHz, $CDCl_3$) δ 1.43 (d, 7.0 Hz, 3H), 2.68 (dd, 8.1 Hz, 15.2 Hz, 1H), 2.78 (dd, 7.0 Hz, 15.2 Hz, 1H), 3.49 (m, 1H), 3.65 (s, 3H), 7.46 (m, 3H), 7.69 (s, 1H), 7.83 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 37.0, 43.1, 52.0, 125.4, 125.8, 125.9, 126.4, 128.0, 128.1, 128.6, 132.8, 134.0, 143.6, 173.3; ESI MS: 246 (M^++NH_4^+); HRMS calculated for $C_{15}H_{20}NO_2$ 246.1494 found 246.1481.

Example 10: Synthesis and Structure of the following bisphosphine:

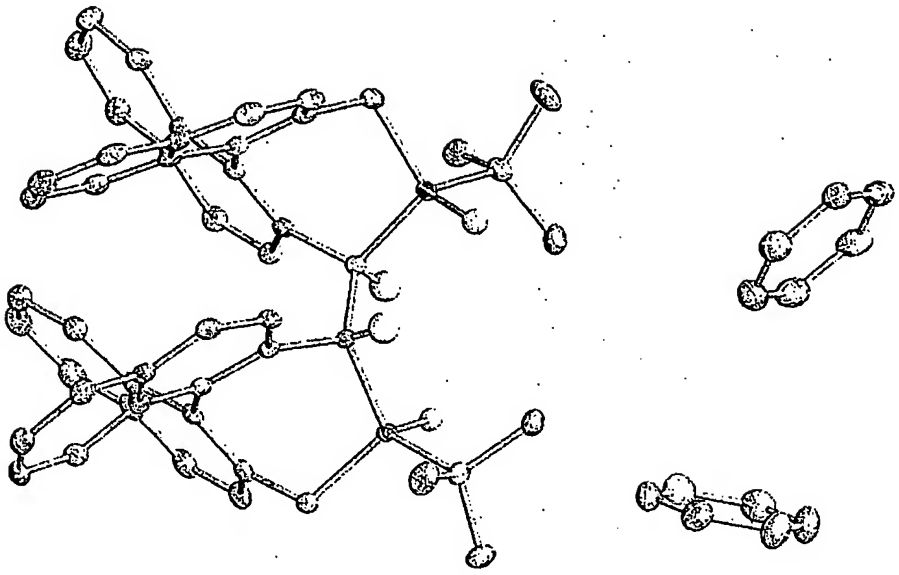
Synthesis and application of TangPhos type ligands



A chiral bisphosphine with the following structure was prepared by the procedure outlined above:

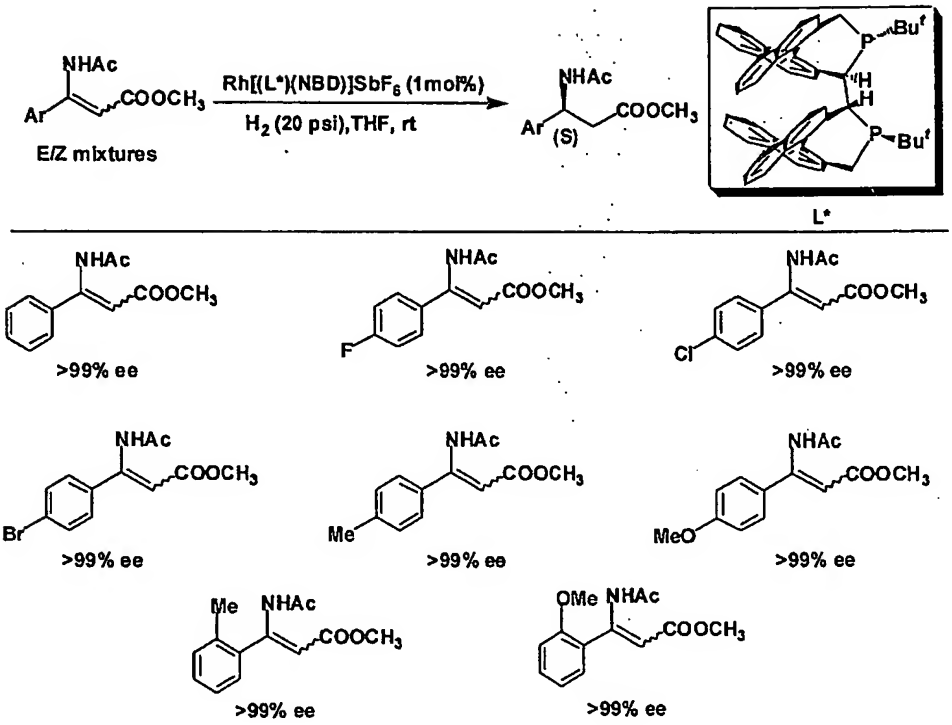


The X-ray structure of the corresponding bisphosphine sulfide was obtained and is shown below:



Further Applications

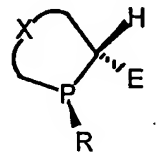
Rh-compound with this ligand is an effective catalyst for hydrogenation of enamides (e.g., E/Z mixture of PhCH(NHAc)CHCOOEt) to make beta amino acids (up to 99% ee has been achieved).



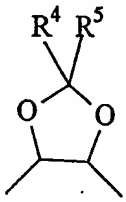
The present invention has been described with particular reference to the preferred embodiments. It should be understood that the foregoing descriptions and examples are only illustrative of the invention. Various alternatives and modifications thereof can be devised by those skilled in the art without departing from the spirit and scope of the present invention. Accordingly, the present invention is intended to embrace all such alternatives, modifications, and variations that fall within the scope of the appended claims.

What is claimed is:

1. A chiral ligand represented by the following formula or its enantiomer:



wherein X is a divalent group selected from the group consisting of: $(CR^4R^5)_n$, $(CR^4R^5)_n$-Z-$(CR^4R^5)_n$ and group represented by the formula:

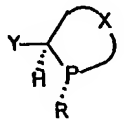


wherein each n is independently an integer from 1 to 6; wherein each R^4 and R^5 is independently selected from the group consisting of: hydrogen, alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, halogen, hydroxy, alkoxy, aryloxy, alkylthio, arylthio and amido; and

wherein Z is selected from the group consisting of: O, S, -COO-, -CO-, O-$(CR^4R^5)_n$-O, CH_2 (C_6H_4), CH_2 (Ar), CH_2(hetereoaryl), alkenyl, CH_2(alkenyl), C_5H_3N, divalent aryl, 2,2'-divalent-1,1'-biphenyl, SiR'_2, PR' and NR^6 wherein each of R' and R^6 is independently selected from the group consisting of: hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, hydroxy, alkoxy, aryloxy, acyl and alkoxycarbonyl;

wherein R is selected from the group consisting of: alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, alkoxy and aryloxy;

wherein E is selected from the group consisting of: PR'_2, PR'R", o-substituted pyridine, oxazoline, chiral oxazoline, CH_2(chiral oxazoline), CR'2(chiral oxazoline), $CH_2PR'_2$, CH_2(o-substituted pyridine), SiR'_3, CR'_2OH and a group represented by the formula:



wherein Y is selected from the group consisting of:

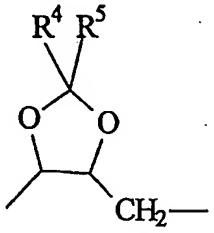
$(CR^4R^5)_m$ and $(CR^4R^5)_m$-Z-$(CR^4R^5)_m$;

wherein each m is independently an integer from 0 to 3; wherein each R^4 and R^5 is independently selected from the group consisting of: hydrogen, alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, halogen, hydroxy, alkoxy, aryloxy, alkylthio, arylthio and amido; and wherein Z is selected from the group consisting of: O, S, -CO-, -COO-, O-$(CR^4R^5)_n$-O, CH_2 (C_6H_4), CH_2 (Ar), CH_2(hetereoaryl), alkenyl, CH_2(alkenyl), C_5H_3N, divalent aryl, 2,2'-divalent-1,1'-biphenyl, SiR'_2, PR' and NR^6 wherein each of R' and R^6 is independently selected from the group consisting of: hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, hydroxy, alkoxy, aryloxy, acyl and alkoxycarbonyl.

2. The chiral ligand of claim 1, wherein:

X is selected from the group consisting of: $(CH_2)_n$ wherein n is from 1 to 6, CH_2OCH_2, CH_2NHCH_2, $CH_2CH(R')CH(R')$, $CH_2CH(OR')CH(OR')$,

$CH_2CH(OH)CH(OH)$, $CH_2NR'CH_2$, $CH_2CH_2NR'CH_2$, $CH_2CH_2OCH_2$ and a group represented by the formula:



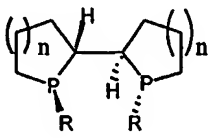
wherein each R^4 and R^5 is independently selected from the group consisting of: hydrogen, alkyl, aryl, substituted alkyl and substituted aryl.

3. The chiral ligand of claim 1, wherein:

Y is selected from the group consisting of: $(CH_2)_n$ wherein n is from 0 to 3, CH_2NHCH_2, CH_2SCH_2, $CH_2PR'CH_2$, CR'2, CO, SiR'_2, C_5H_3N, C_6H_4, alkylene, substituted alkylene, 1,2-divalent arylene, 2,2'-divalent-1,1'-biphenyl, substituted aryl, hetereoaryl and ferrocene.

4. The chiral ligand of claim 1, wherein the ligand is in the form of a phosphine borane, phosphine sulfide or phosphine oxide.

5. A chiral ligand represented by the formula and its enantiomer:



n = 0, 1, 2

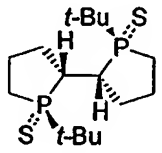
wherein R is selected from the group consisting of: alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, alkoxy and aryloxy; and

wherein n is from 0 to 2.

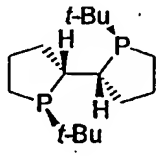
6. The chiral ligand of claim 5, wherein n is 0, 1 or 2, and R is selected from the group consisting of: CH_3, Et, iPr, t-Bu, 1-adamantyl, Et_3C, cyclo-C_5H_9, cyclo-C_6H_{11}, phenyl, p-tolyl, 3,5-dimethylphenyl, 3,5-di-t-butyl phenyl, ortho-anisyl and naphthyl.

7. The chiral ligand of claim 5, wherein the ligand is in the form of a phosphine borane, phosphine sulfide or phosphine oxide.

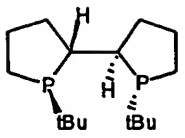
8. A chiral ligand represented by the formula and its enantiomer:



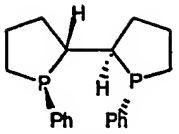
9. A chiral ligand represented by the formula and its enantiomer:



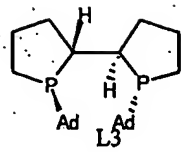
10. A chiral ligand selected from the group consisting of compounds represented by formulas L1 through L52 and their enantiomers:



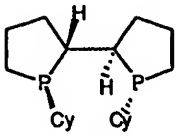
L1



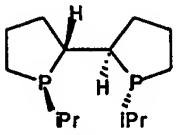
L2



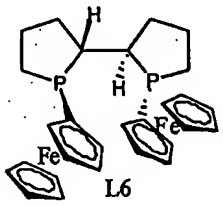
L3



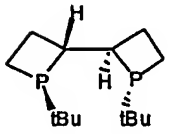
L4



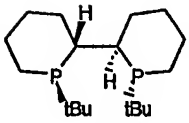
L5



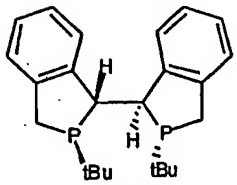
L6



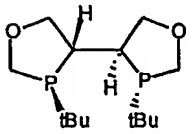
L7



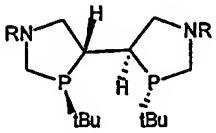
L8



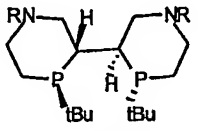
L9



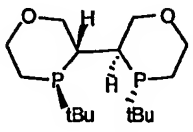
L10



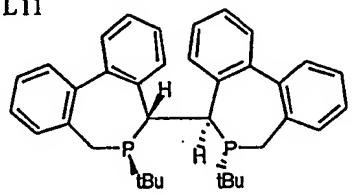
L11



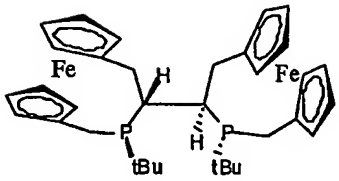
L12



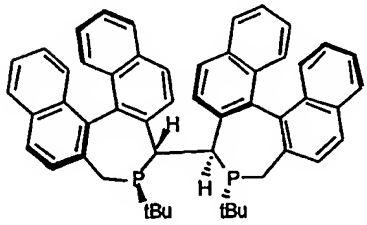
L13



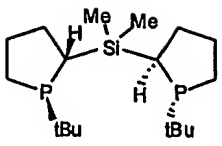
L14



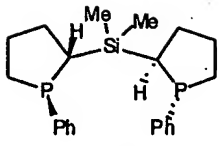
L15



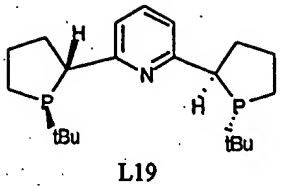
L16



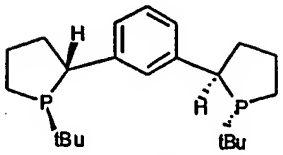
L17



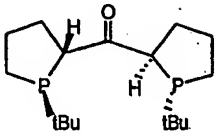
L18



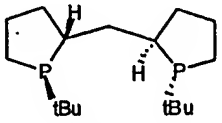
L19



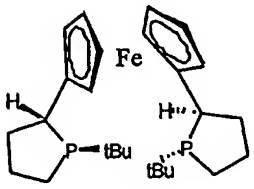
L20



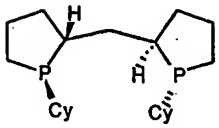
L21



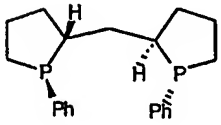
L22



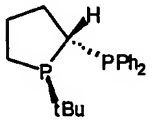
L23



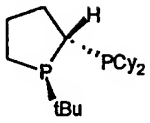
L24



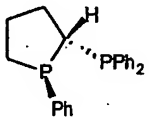
L25



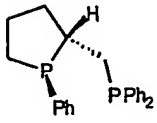
L26



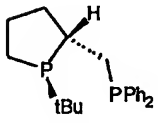
L27



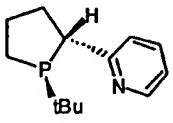
L28



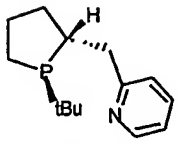
L29



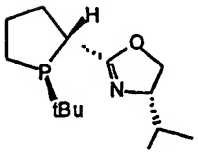
L30



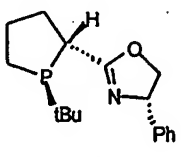
L31



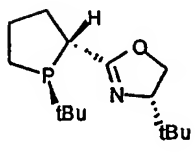
L32



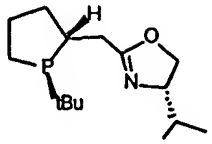
L33



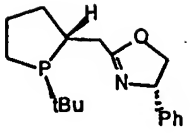
L34



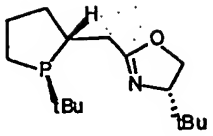
L35



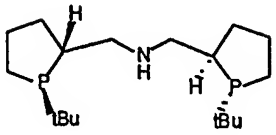
L36



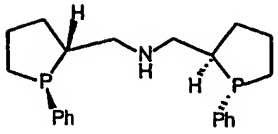
L37



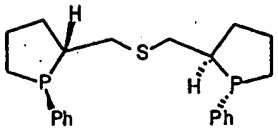
L38



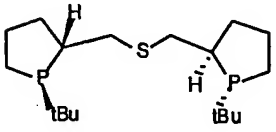
L39



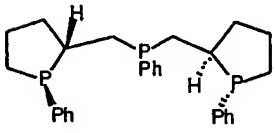
L40



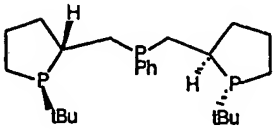
L41



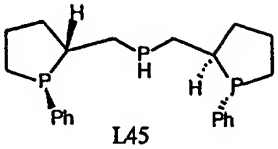
L42



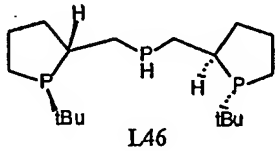
L43



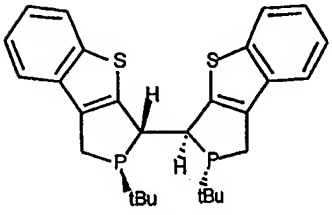
L44



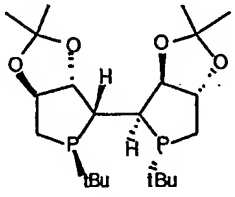
L45



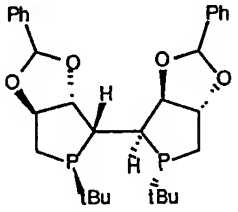
L46



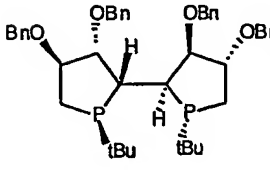
L47



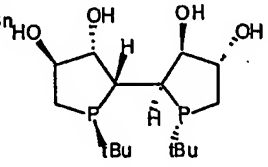
L48



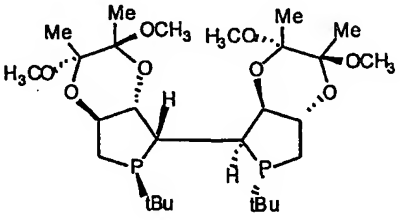
L49



L50



L51

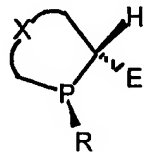


L52

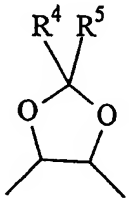
5

11. A catalyst prepared by a process comprising:

contacting a transition metal salt, or a complex thereof, and a chiral ligand selected from the group consisting of compounds represented by the formula or its enantiomer:



wherein X is a divalent group selected from the group consisting of: $(CR^4R^5)_n$, $(CR^4R^5)_n$-Z-$(CR^4R^5)_n$ and group represented by the formula:

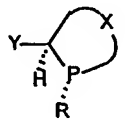


wherein each n is independently an integer from 1 to 6; wherein each R^4 and R^5 is independently selected from the group consisting of: hydrogen, alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, halogen, hydroxy, alkoxy, aryloxy, alkylthio, arylthio and amido; and

wherein Z is selected from the group consisting of: O, S, -COO-, -CO-, O-$(CR^4R^5)_n$-O, CH_2 (C_6H_4), CH_2 (Ar), CH_2(hetereoaryl), alkenyl, CH_2(alkenyl), C_5H_3N, divalent aryl, 2,2'-divalent-1,1'-biphenyl, SiR'_2, PR' and NR^6 wherein each of R' and R^6 is independently selected from the group consisting of: hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, hydroxy, alkoxy, aryloxy, acyl and alkoxycarbonyl;

wherein R is selected from the group consisting of: alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, alkoxy and aryloxy;

wherein E is selected from the group consisting of: PR'_2, PR'R", o-substituted pyridine, oxazoline, chiral oxazoline, CH_2(chiral oxazoline), CR'2(chiral oxazoline), $CH_2PR'_2$, CH_2(o-substituted pyridine), SiR'_3, CR'_2OH and a group represented by the formula:



wherein Y is selected from the group consisting of:

$(CR^4R^5)_m$ and $(CR^4R^5)_m$-Z-$(CR^4R^5)_m$;

wherein each m is independently an integer from 0 to 3;

wherein each R^4 and R^5 is independently selected from the group consisting of: hydrogen, alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, halogen, hydroxy, alkoxy, aryloxy, alkylthio, arylthio and amido; and wherein Z is selected from the group consisting of: O, S, -CO-, -COO-, O-$(CR^4R^5)_n$-O, CH_2 (C_6H_4), CH_2 (Ar), CH_2(hetereoaryl), alkenyl, CH_2(alkenyl), C_5H_3N, divalent aryl, 2,2'-divalent-1,1'-biphenyl, SiR'_2, PR' and NR^6 wherein each of R' and R^6 is independently selected from the group consisting of: hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, hydroxy, alkoxy, aryloxy, acyl and alkoxycarbonyl.

12. The catalyst of claim 11, wherein said catalyst is a racemic mixture of enantiomers.

13. The catalyst of claim 11, wherein said catalyst is a non-racemic mixture of enantiomers.

14. The catalyst of claim 31, wherein said catalyst is one of the enantiomers.

15. The catalyst of claim 11, wherein said transition metal is selected from the group consisting of: Ag, Pt, Pd, Rh, Ru, Ir, Cu, Ni, Mo, Ti, V, Re and Mn.

16. The catalyst of claim 15, wherein said transition metal is selected from the group consisting of: Cu, Ag, Ni, Pt, Pd, Rh, Ru and Ir.

17. The catalyst of claim 11, wherein said transition metal salt, or complex thereof, is selected from the group consisting of: AgX; Ag(OTf); $Ag(OTf)_2$; AgOAc; $PtCl_2$; H_2PtCl_4; $Pd_2(DBA)_3$; $Pd(OAc)_2$; $PdCl_2(RCN)_2$; $(Pd(allyl)Cl)_2$; $Pd(PR_3)_4$; $(Rh(NBD)_2)X$; (Rh (NBD)Cl)$_2$; $(Rh(COD)Cl)_2$; $(Rh(COD)_2)X$; Rh(acac)$(CO)_2$; Rh(ethylene)$_2$(acac); $(Rh(ethylene)_2Cl)_2$; $RhCl(PPh_3)_3$; $Rh(CO)_2Cl_2$; $RuHX(L)_2$(diphosphine), $RuX_2(L)_2$ (diphosphine), Ru(arene)X_2(diphosphine), Ru(aryl group)X_2; Ru(RCOO)$_2$(diphosphine); Ru(methallyl)2(diphosphine); Ru(aryl group)$X_2(PPh_3)_3$; Ru(COD)(COT); Ru(COD)(COT)X; RuX_2(cymen); $Ru(COD)_n$; Ru(aryl group)X_2(diphosphine); $RuCl_2$(COD); $(Ru(COD)_2)X$; RuX_2(diphosphine); $RuCl_2(=CHR)(PR'_3)_2$; $Ru(ArH)Cl_2$; Ru(COD)(methallyl)$_2$; (Ir $(NBD)_2Cl)_2$; $(Ir(NBD)_2)X$; $(Ir(COD)_2Cl)_2$; $(Ir(COD)_2)X$; CuX $(NCCH_3)_4$; Cu(OTf); $Cu(OTf)_2$; Cu(Ar)X; CuX; $Ni(acac)_2$; NiX_2; $(Ni(allyl)X)_2$; $Ni(COD)_2$; $MoO_2(acac)_2$; $Ti(OiPr)_4$; $VO(acac)_2$; $MeReO_3$; MnX_2 and $Mn(acac)_2$;

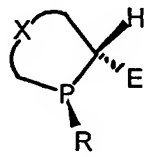
wherein each R and R' is independently selected from the group consisting of: alkyl or aryl; Ar is an aryl group; and X is a counteranion.

18. The catalyst of claim 17, wherein L is a solvent and wherein said counteranion X is selected from the group consisting of: halogen, BF_4, $B(Ar)_4$ wherein Ar is fluorophenyl or 3,5-di-trifluoromethyl-1-phenyl, ClO_4, SbF_6, PF_6, CF_3SO_3, RCOO and a mixture thereof.

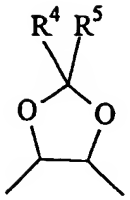
19. The catalyst of claim 11, prepared in situ or as an isolated compound.

20. A process for preparation of an asymmetric compound comprising:

contacting a substrate capable of forming an asymmetric product by an asymmetric reaction and a catalyst prepared by a process comprising: contacting a transition metal salt, or a complex thereof, and a chiral ligand selected from the group consisting of compounds represented by the formula or its enantiomer:



wherein X is a divalent group selected from the group consisting of: $(CR^4R^5)_n$, $(CR^4R^5)_n$-Z-$(CR^4R^5)_n$ and group represented by the formula:

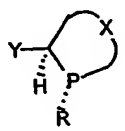


wherein each n is independently an integer from 1 to 6; wherein each R^4 and R^5 is independently selected from the group consisting of: hydrogen, alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, halogen, hydroxy, alkoxy, aryloxy, alkylthio, arylthio and amido; and

wherein Z is selected from the group consisting of: O, S, -COO-, -CO-, $O-(CR^4R^5)_n-O$, CH_2 (C_6H_4), CH_2 (Ar), CH_2(hetereoaryl), alkenyl, CH_2(alkenyl), C_5H_3N, divalent aryl, 2,2'-divalent-1,1'-biphenyl, SiR'_2, PR' and NR^6 wherein each of R' and R^6 is independently selected from the group consisting of: hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, hydroxy, alkoxy, aryloxy, acyl and alkoxycarbonyl;

wherein R is selected from the group consisting of: alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, alkoxy and aryloxy;

wherein E is selected from the group consisting of: PR'_2, PR'R", o-substituted pyridine, oxazoline, chiral oxazoline, CH_2(chiral oxazoline), CR'2(chiral oxazoline), $CH_2PR'_2$, CH_2(o-substituted pyridine), SiR'_3, CR'_2OH and a group represented by the formula:



wherein Y is selected from the group consisting of:

$(CR^4R^5)_m$ and $(CR^4R^5)_m$-Z-$(CR^4R^5)_m$;

wherein each m is independently an integer from 0 to 3;

wherein each R^4 and R^5 is independently selected from the group consisting of: hydrogen, alkyl, aryl, substituted alkyl, substituted aryl, hetereoaryl, ferrocenyl, halogen, hydroxy, alkoxy, aryloxy, alkylthio, arylthio and amido; and wherein Z is selected from the group consisting of: O, S, -CO-, -COO-, O-$(CR^4R^5)_n$-O, CH_2 (C_6H_4), CH_2 (Ar), CH_2(hetereoaryl), alkenyl, CH_2(alkenyl), C_5H_3N, divalent aryl, 2,2'-divalent-1,1'-biphenyl, SiR'_2, PR' and NR^6 wherein each of R' and R^6 is independently selected from the group consisting of: hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, hydroxy, alkoxy, aryloxy, acyl and alkoxycarbonyl.

21. The process of claim 20, wherein said asymmetric reaction is selected from the group consisting of: hydrogenation, hydride transfer, allylic alkylation, hydrosilylation, hydroboration, hydrovinylation, hydroformylation, olefin metathesis, hydrocarboxylation, isomerization, cyclopropanation, Diels-Alder reaction, Heck reaction, isomerization, Aldol reaction, Michael addition; epoxidation, kinetic resolution and [m+n] cycloaddition wherein m = 3 to 6 and n = 2.

22. The process of claim 21, wherein said asymmetric reaction is hydrogenation and said substrate is selected from the group consisting of: imine, ketone, ethylenically unsaturated compound, enamine, enamide and vinyl ester.

23. The process of claim 21, wherein said asymmetric reaction is an iridium, ruthenium, rhenium or palladium-catalyzed hydrogenation of an olefin, imine, enamide or ketone.

24. A process for preparing (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl -[2,2']-diphospholanyl-1,1'-disulfide comprising the steps of:

asymmetrically deprotonating a 1-alkyl-phospholane-1-sulfide with n-butyllithium/(-)-sparteine in a solvent to produce an anion of said 1-alkyl-phospholane-1-sulfide; and

contacting said anion of said 1-alkyl-phospholane-1-sulfide and $CuCl_2$ to oxidatively couple said anion of said 1-alkyl-phospholane-1-sulfide and produce a reaction mixture comprising said (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide.

25. The process of claim 24, wherein said alkyl is *tert*-butyl.

26. The process of claim 24, further comprising the step of:

recrystallizing said (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide from said reaction mixture.

27. The process of claim 26, further comprising the step of:

contacting said (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide and hexachlorodisilane in a solvent to produce (*1S, 1S', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl.

28. A process for preparing (*1S, 1S', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl comprising the steps of:

asymmetrically deprotonating a 1-alkyl-phospholane-1-sulfide with n-butyllithium/(-)-sparteine in a solvent to produce an anion of said 1-alkyl-phospholane-1-sulfide;

contacting said anion of said 1-alkyl-phospholane-1-sulfide and $CuCl_2$ to oxidatively couple said anion of said 1-alkyl-phospholane-1-sulfide and produce a reaction mixture comprising (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide;

recrystallizing said (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide from said reaction mixture; and

contacting said (*1R, 1R', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl-1,1'-disulfide and hexachlorodisilane in a solvent to produce (*1S, 1S', 2R, 2R'*)-1,1'-di-alkyl-[2,2']-diphospholanyl.

29. The process of claim 28, wherein said alkyl is *tert*-butyl.